Study on the Location of the Activated Cerebellum Regions in Manual Movement Related to Handedness

Qing Gao and Hua-Fu Chen

Abstract—The present study used functional magnetic resonance imaging (fMRI) to study the activated site in the cerebellum during bi-hand movement and uni-hand movement, and the lateralization of the cerebellum in hand movement. The coordinates of the peak activation in the CRB were compared using statistical tests, and the results in the primary motor cortex (PMC) were presented as comparison. The results showed a significant difference in cerebellum during bi-hand movement comparing the right-handed with the left-handed subjects. When comparing the right-handed subjects and left-handed subjects during right-hand movement, the significantly different coordinate in dorsal/ventral orientation was observed. The results also showed the different activated site during bi-hand movement and non-dominant hand movement. Our study took the point of view of the lateralization in cerebellum, and the results demonstrated the different site of the peak activation in cerebellum during bi-hand movement and uni-hand movement, which suggested that the handedness also existed in the cerebellum.

Index Terms—Cerebellum, functional magnetic resonance imaging, laterality, peak activation.

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1. Introduction

The cerebellum (CRB) and the primary motor cortex (PMC) have been postulated to make fundamental and synergistic contributions to the control of movement. The research has been done through the eyes of molecular, cellular, circuit and behavioral levels\textsuperscript{[1][2]}. When focused on the functions of the two regions, the cerebellum has been postulated to play roles in ‘on line’ correction of error, coordination of multi-joint movements, motor skill acquisition, visual guidance of movement, specification of movement velocity, and the elaboration of internal models. On the other hand, the PMC has been hypothesized to be a controller of muscles and/or joints, primarily responsible for the specification of force and/or muscle activation\textsuperscript{[3]}.

For the cerebellum, two key components are established during cerebellar development: a highly specific and uniform laminar arrangement of cells in the cerebellar cortex, and an equally specific and uniform microcircuitry\textsuperscript{[4]}. The cerebellum receives input from a wide variety of sources, including areas of frontal, prefrontal, cingulate and posterior parietal cortex. This information was thought to be funneled into the motor system to generate and control movement\textsuperscript{[1]}. Different cerebellar regions are likely to be involved in the control of these movement types. Medial cerebellar structures are probably more important for walking and balance, whereas intermediate and lateral cerebellar structures for reaching, pinching and catching\textsuperscript{[2]}.

The prior studies hypothesized that the cerebellum is a clock within the central nervous system (CNS)\textsuperscript{[4]}. Moreover, a new findings suggested that the cerebellum functions as a sensorimotor predictor\textsuperscript{[5]}. The cerebellum plays a crucial way in the manual movement coordination.

Handedness is a prominent behavioral asymmetry that has been quantitatively studied in the PMC by the volume of the activated voxels, the intensity of the activated signals, and the activated area ratio which was named as hemispheric index\textsuperscript{[5]-[8]}. In the cerebellum, the handedness was studied mostly from the point of view of morphology. Magnetic resonance (MR) imaging volumetry\textsuperscript{[9]}, asymmetry quotient (AQ) and computation of cerebellar torque index (CTI) were defined as the function of the volume of region of interest (ROI) in the cerebellum in nonhuman primates\textsuperscript{[10]} or in human\textsuperscript{[11][12]} to detect the asymmetry of the cerebellum. However, whether there is functional effect of handedness in the cerebellum has received limited attention. In 1985, Fox et al.\textsuperscript{[13]} observed that the self-paced finger movements in association with rapidly alternation movements of flexion and extension of the fingers activated only the ipsilateral anterior cerebellum. The study in functional connectivity...
concluded that the left-handed subjects showed higher cerebellar-prefrontal, cerebellar-parietal, and cerebellar-temporal functional connectivity, and lower cerebellar-limbic connectivity\cite{14}.

In the present study, we addressed the problem of whether the human cerebellum was involved in hand movement with handedness. Bi-hand movement and uni-hand movement, which are simple kinds of bimanual coordination, were performed in the study. The present study focused on the coordinates of the peak activation, and investigated whether there are differences between bi-hand movement and uni-hand movement for the right- and left-handed subjects, respectively. Then the difference of the site between right- and left-handed subjects was discussed.

2. Methods

2.1 Subjects

The study was approved by the local ethical committees, and informed written consent was obtained from all subjects. Twelve subjects participated in the study, including six healthy right-handed (3 male, 3 female) and six healthy left-handed (3 male, 3 female). All subjects were healthy, with no history of psychiatric or neurological illness. Their ages were from 16 to 26 (mean age=20) and had a mean education of 14 years. Handedness was evaluated with the Edinburgh Handedness Inventory (EHI), which produced a laterality quotient that varies from −100 (strongly left handed) to 0 (no hand preference) to 100 (strongly right handed). The average score on the Edinburgh inventory was 91.67 with a standard deviation of 8.94.

2.2 Data Acquisition

Imaging data were acquired on a 3.0 Tesla GE scanner (EXCITE, General Electric, Milwaukee, USA) with an 8 channel phase array head coil. The acquisition parameters were: TR = 2.0 s, TE = 30 ms, Flip angle = 90°, field of view (FOV) = 24 cm × 24 cm, matrix size = 64 × 64, and voxel size = 3.75 mm × 3.75 mm × 5 mm.

2.3 Task Procedures

The subjects were trained to grip their hands with the frequency of 1 Hz before the task. In the scanner, visual stimuli were computer-generated by E-prime and projected onto an opaque screen located at the subject’s head. All subjects performed the following three tasks: 1) bi-hand gripping, 2) right-hand gripping, and 3) left-hand gripping. When performing the bi-hand gripping, subjects were instructed to grip both of their hand simultaneously. During the single hand task, subjects were instructed to relax the opposite hand, gripped their left or right hand separately. All of the gripping tasks in the current experiment were a block designed paradigm, triggered by the cross in the middle of the screen. Each run consisted of 5 blocks of a gripping condition alternating with rest. During rest periods, subjects were instructed to remain still and fixate on the center of the screen with an asterisk. The gripping condition and rest periods were each 20 seconds in duration and each consisted of ten images.

2.4 Data Analysis

The first 10 time points of the resting state were discarded for scanner calibration and for the subjects to get used to the circumstance, leaving five blocks of 100 time points for analysis. The functional images were preprocessed and analyzed using statistical parametric mapping (SPM, http://www.fil.ion.ucl.ac.uk/spm). All remained images were realigned to the first image in the series to correct for rotation and translation of the participant’s head movement during the scanning session. Subsequently, the preprocessing of the images was performed in the order of slice timing, spatial normalization and smoothing. After the pre-processing, the voxel size was normalized into a standard stereotaxic space at 2 mm × 2 mm × 2 mm, and the voxel coordinates were transformed from the Montreal Neurological Institute (MNI) coordinates to the Talairach coordinates. The time series for each voxel was analyzed using a general linear model (GLM). According to one sample t-test statistical method (p<0.01, corrected for the family-wise error (FWE)) provided by SPM2 software, the results of the active area in cortex were identified for each task. Subsequently, in order to extend inferences based on the individual statistical analyses to the general population from which the subjects were drawn, a random-effect analysis was performed. A one-sample t-test (q = 0.05, false discovery rate (FDR) corrected) was performed across subjects on their activated images.

The coordinates of the peak activation in the PMC and the cerebellum were obtained by the statistical parametric maps. Paired-sample t-test was performed to compare the differences of the coordinates.

3. Results

The activated areas obtained by group analysis are shown in Fig. 1 and Fig. 2 for the right-handed subjects and the left-handed subjects, respectively (q = 0.05, FDR corrected). By comparing (b) and (c) in the first parallel of Fig. 1, we could easily observe the handedness in the cerebellum. The peak site was defined as the single most significantly activated voxel. Paired-sample t-tests were used to compare: 1) the coordinates in the left PMC for bi-hand movement versus right-hand movement, 2) the coordinates in the right PMC for bi-hand movement versus left-hand movement, 3) the coordinate in the cerebellum for bi-hand movement versus uni-hand movement, and 4) the coordinate in the cerebellum for left-hand movement versus right-hand movement. The comparisons were performed for the right-handed and the left-handed subjects respectively, and then the contrast result between the right- and left-handed subjects was discussed.
Fig. 1. Activated areas obtained by group analysis for the right-handed subjects: (a) bi-hand movement, (b) left-hand movement, and (c) right-hand movement.

Fig. 2. Activated areas obtained by group analysis for the left-handed subjects: (a) bi-hand movement, (b) left-hand movement, and (c) right-hand movement.

Table 1: Brain activation for the group analysis results in right-handed subjects

<table>
<thead>
<tr>
<th>Activation</th>
<th>Coordinates</th>
<th>Voxels</th>
<th>t-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bi-hand movement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LPMC</td>
<td>−32 −26 60</td>
<td>386</td>
<td>17.26</td>
</tr>
<tr>
<td>RPMC</td>
<td>34 −21 66</td>
<td>380</td>
<td>14.60</td>
</tr>
<tr>
<td>CRB</td>
<td>13 −60 −21</td>
<td>408</td>
<td>12.36</td>
</tr>
<tr>
<td>Right-hand movement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LPMC</td>
<td>−32 −26 62</td>
<td>735</td>
<td>18.45</td>
</tr>
<tr>
<td>CRB</td>
<td>19 −52 −26</td>
<td>258</td>
<td>13.52</td>
</tr>
<tr>
<td>Left-hand movement</td>
<td></td>
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<td></td>
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<tr>
<td>RPMC</td>
<td>34 −22 65</td>
<td>609</td>
<td>17.76</td>
</tr>
<tr>
<td>CRB</td>
<td>−17 −56 −22</td>
<td>208</td>
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</tr>
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</table>

Abbreviations: LPMC: left primary motor cortex; RPMC: right primary motor cortex; CRB: cerebellum.

Table 1 shows the coordinates of the significantly activated peak in SPM2, where the coordinates use radiological convention: $x$ represents right/left (+/−), $y$ represented rostral/caudal (+/−), and $z$ represents dorsal/ventral (+/−).

### 3.1 Results of the Right-Handed Subjects

The Talairach coordinates of the peak activation in the PMC and the cerebellum for right-handed subjects are shown in Table 1, along with the cluster results of group analysis. Using paired-sample $t$-test, the results showed that the sites in both left PMC and right PMC during bi-hand movement were comparable to that during uni-hand movement. The significant difference was observed in the cerebellum. When comparing coordinates of the peak activation in bi-hand movement with left-hand movement in the cerebellum, there was significant difference in $x$-coordinate ($p = 0.0079$). When comparing bi-hand movement versus right-hand movement, the significant difference was observed in $z$-coordinate ($p = 0.0482$), whereas slight difference in $x$-coordinate ($p = 0.0844$) and $y$-coordinate ($p = 0.0815$). In right-hand movement versus left-hand movement, the different site was significant in $x$-coordinate ($p = 0.0012$), comparable in $y$-coordinate ($p = 0.1680$) and $z$-coordinate ($p = 0.0624$).

### 3.2 Results of the Left-Handed Subjects

The Talairach coordinates of the peak activation in the PMC and the cerebellum, and the cluster results of group analysis for left-handed subjects are shown in Table 2. The results of $t$-test showed that the sites in both left PMC and right PMC were comparable in bi-hand movement versus uni-hand movement, which was the same with that of the right-handed subjects. The significant difference also
Table 2: Brain activation for the group analysis results in left-handed subjects

<table>
<thead>
<tr>
<th>Activation</th>
<th>Coordinates</th>
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<th>t-values</th>
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<tbody>
<tr>
<td></td>
<td>x</td>
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<td>z</td>
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<tr>
<td>Bi-hand movement</td>
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<tr>
<td>RPMC</td>
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<tr>
<td>Right-hand movement</td>
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<tr>
<td>LPMC</td>
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<td>-20</td>
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<td>Left-hand movement</td>
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4. Conclusions

In the studies of bi-manual movement, there were so many quantitative results of the asymmetrical intensity and cluster size in the PMC related to handedness by the method of fMRI. In the current study, no significant differences in the peak activation in the PMC was found when comparing right and left hemispheres (absolute values were used when comparing x-coordinate results), which was concordant with the prior results[15]. Also the sites were not sensitive to handedness. The results implied that the handedness representation in the PMC was not based on the site but based on the intensity and cluster size of the activated regions in brain.

Interestingly, in the cerebellum, the site was significantly different when comparing the right-handed subjects versus the left-handed subjects during bi-hand movement. In right-handed subjects, the coordinate of peak activation was (13, -60, -21) during bi-hand movement, which was sited in anterior lobe of the right cerebellum; whereas in left-handed subjects, the coordinate was (-8, -54, -17), which was sited in the left cerebellum. The significant difference was observed in x-coordinate (p=0.0084), which suggested the handedness also existed in the cerebellum. The results of the current study suggested that the activation of the cerebellum during bi-hand movements occurred at a site distinct from the non-dominant hand movements. The difference was primarily significant in x-coordinate, which represented right/left orientation. In the right-handed subjects, the significant difference appeared during bi-hand versus left-hand movement (p=0.0079 in x-coordinate); while in the left-handed subjects, the significant difference appeared during bi-hand versus right-hand movement (p=0.0206 in x-coordinate). Considering the function of the cerebellum as the bimanual coordination[1], our results were concordant with the prior studies that the cerebellum contributed to non-motor, as well as motor function, and these two functions appeared to be distributed within different regions of the human cerebellar cortex[11]. Because bi-hand movement and uni-hand movement are simple kinds of bimanual coordination, the results demonstrated that the site activated during bi-hand movement control differed from that during non-dominant hand movement control in right/left orientation, which implied the lateralization in the cerebellum.

In right-hand movement, the peak activation representation was in anterior lobe of the right cerebellum both in the right-handed and left-handed subjects, and mirror versed in left-hand movement. The results were concordant with the prior studies that cerebellar control is ipsilateral[16], and extended the findings to the lateralization of the cerebellum.

The handedness was also observed in z-coordinate, which represented the dorsal/ventral orientation. During right-hand movement, significant difference between the right-handed and left-handed subjects was observed in z-coordinate (p=0.0098) in the cerebellum, implying the lateralization in the dorsal/ventral orientation.

In sum, our study took the point of view of the handedness in the cerebellum, and compared with the handedness in the PMC. The current results suggested the different site of the peak activation in the cerebellum during bi-hand movement and uni-hand movement. Furthermore, the lateralization was found in the cerebellum.

References


Qing Gao was born in Sichuan Province, China, in 1977. She received the M.S. degree from the Beijing Normal University, Beijing, China, in 2002. She is currently pursuing the Ph.D. degree with the School of Life Science and Technology, University of Electronic Science and Technology of China (UESTC). Her research interests include diffusion-weighted imaging at high b-value, functional magnetic resonance imaging, and signal and image processing.

Hua-Fu Chen was born in Sichuan Province, China, in 1967. He received the Ph.D. degree in biomedical engineering from UESTC in 2004. He is the author or coauthor of more than 30 SCI index scientific papers. He is currently a professor with the School of Life Science and Technology, UESTC. His research interests include independent component analysis, functional magnetic resonance imaging, and signal and image processing.