Human primary motor cortex shows hemispheric specialization for speech

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Hemispheric specialization is a prominent characteristic of the human brain. Should the ‘dominant’ hemisphere possess differential neural organization for language production in the ‘higher order’ cortex, it would be rational to consider that the primary motor cortex may also show similar hemispheric specialization for speech production. In order to test this hypothesis, we investigated the spatial distribution of neural activities associated with phonation (M1p), silent tongue motion (M1t), and vocalization (M1v) within the primary motor cortex, utilizing independent component–cross correlation–sequential epoch analysis of high-field functional magnetic resonance imaging time series. While M1t showed no significant differences between the two hemispheres, M1p and M1v exhibited significant hemispheric differences. The study demonstrated direct evidence that human primary motor cortex possesses clear-cut hemispheric specialization similar to that observed for the higher order cortices.

Keywords: functional magnetic resonance imaging, hemispheric specialization, independent component–cross correlation–sequential epoch analysis, motor cortex, speech

Introduction
Hemispheric specialization, as most clearly illustrated by language, is a prominent characteristic of the human brain. Given that neural organization for language production within the higher-order cortex of the dominant hemisphere is distinct, it would be reasonable to consider that the primary motor cortex (M1) may also possess hemispheric specialization for the purposes of speech production. Several lines of indirect evidence indeed support such a possibility. Significantly greater cerebral blood flow in the left M1 than the right during speech production has suggested different activities between left and right M1 [1]. Compared with singing, activation during speech is more lateralized to the left hemisphere, especially to the lower M1 area [2]. Speech-related modulation of motor evoked potentials is lateralized toward the dominant hemisphere for language in nonmusicians [3]. Speech interruption by transcranial magnetic stimulation is more prominent over the left hemisphere [4].

The orofacial representation area of M1 functionally connects with the inferior frontal gyrus [5]. It is convincing that such cortico-cortical connection between the higher-order cortex for language production and M1 relates to distinct hemispheric specialization within M1 for speech production. There is also cytoarchitectural evidence of interhemispheric asymmetry of M1 [6]. Nevertheless, there is currently no direct evidence that M1 possesses hemispheric specialization even though previous studies have segregated vocalization representational areas of M1 into regions associated with the phases of vocalization (e.g. phonation, articulation or respiration) [7,8].

In this study, we investigated spatial distributions of speech-related areas within M1, using independent component–cross correlation–sequential epoch (ICS) analysis [9,10] of high-field (3.0 T) functional magnetic resonance imaging (fMRI) time series.

Materials and methods
Eighteen right-handed normal subjects (18–43 years old, nine women and nine men) participated in the study. The study was carried out in accordance with the human research guidelines of the Internal Review Board of the University of Niigata. A Signa 3.0 T (GE Medical System, Waukesha, Wisconsin, USA) research imaging system was utilized for all imaging. For functional imaging, gradient echo-planar images were obtained using the following parameters: field of view 20 × 20 cm; matrix 64 × 64; slice thickness 5 mm; repetition time 1000 ms; echo time 30 ms; flip angle 70°. Each slab was restricted to 30 mm to maintain high-field homogeneity. Spatial resolution was approximately 3 × 3 × 5 mm³.

Participants performed three types of motor task (Fig. 1a): [T] articulatory tongue movements without phonation
(producing tongue movements for the syllables /lalelilulelolalo/ silently without sound), [P] phonation without articulatory tongue movements (voicing Japanese vowel /e/), and [V] simultaneous phonation and articulatory tongue movements (voicing the syllables /lalelilulelolalo/). The combinations of syllables require rapid and precise vertical tongue movements, and are generally used for training fluent articulation. In contrast, phonation of the Japanese vowel /e/ hardly requires any tongue movements. Dynamic fast gradient echo imaging visualized movements of the tongue, pharynx, and larynx, assuring correct performance. Each fMRI imaging session consisted of nine 30-s epochs in the sequence of r-T-P-V-r-T-P-V-r. Accordingly, three model functions primarily reflecting (1) tongue motion (M1t), (2) motion for phonation (M1p), and (3) motion for vocalization (M1v) could be analyzed (Fig. 1b). Activation maps of all participants were spatially normalized onto a common standard space (Fig. 3).

Data from individual participants were analyzed by fast-ICS analysis. In brief, fMRI data consisting of 270 consecutive echo-planar images per slice were blindly separated into 270 spatially independent components by independent component analysis (ICA) on a 64-CPU SGI Origin 2000 supercomputer system (Mountain View, California, USA). Subsequently, the unmixed time series were correlated to three delayed-boxcar (6s) functions that modeled fMRI signal responses to silent articulation, phonation, and simultaneous articulation and phonation (Fig. 1b), using a cutoff correlation coefficient threshold of correlation coefficient >0.55. The spatial distribution was separately subjected to two different types of cluster analysis, hierarchical [11] and nonhierarchical [12]. Distances from components to their center of gravity and z coordinates in each cluster were tested by one-way analyses of variance to confirm each clustering. Coordinates correspond to the standard atlas of Montreal Neurological Institute’s template (MNI152).

Results

M1 activation in speech production clearly segregated into spatially independent and functionally distinct components corresponding to the three modeled functions, silent articulation (M1t), phonation (M1p), and simultaneous articulation and phonation (M1v) (Fig. 2). Activation of all three components mapped within the lower part of the primary motor cortex inferior to the hand area (Fig. 3). While M1t showed no significant differences between the two hemispheres, M1p and M1v exhibited significant hemispheric differences. Components for M1p and M1v each formed two distinct clusters, inferior and superior, in the left hemisphere. Cluster analysis by statistical methods [11,12] confirmed the asymmetric nature of the clustering (Fig. 4, Table 1). Analysis of M1v using the K means method at the three-cluster level (k=3), demonstrated that left M1
consisted of two clusters, while right M1 comprised a single cluster. Subsequently, at the four-cluster level \((k=4)\), three clusters were obtained in the left M1, dividing the superior cluster at the three-cluster level into two clusters, while the cluster in right M1 remained a single cluster without further separation. Analysis of M1p using both the Ward method and \(k\)-means method at the four-cluster level \((k=4)\) revealed two clusters formed in both left and right M1. The average distance of components from the center of the respective clusters, however, showed that superior and inferior M1p in left M1 formed significantly smaller clusters [superior M1p: \(F(1, 40)=12.7, P=0.00095\); inferior M1p: \(F(1, 19)=6.83, P=0.017\)]. Moreover, comparing the \(z\) coordinates of the left and right clusters, the distance between superior and inferior M1p in left M1 was significantly greater [superior M1p: left mean = 42, right mean = 43, \(F(1, 40)=0.666, P=0.42\); inferior M1p: left mean = 21, right mean = 29, \(F(1, 19)=7.48, P=0.013\)] than the distance between the corresponding clusters on the right. The Euclidean distances between the mean coordinates of the inferior and superior clusters were found to be 31 and 26 mm for left M1p and left M1v, respectively (Fig. 5). Indeed, the distances between the superior and inferior clusters, for M1p and M1v respectively (Fig. 3), were significantly larger than the distance between the mean coordinates of the foot and fist region of 22 mm [13].

**Discussion**

The success of the current study is largely due to the unique strengths of ICS analysis. ICA [14,15] is a novel statistical signal processing technique, the application of which has recently received much attention in research and industrial fields. Compared with principal component analysis, which removes second-order correlations from observed signals, ICA further removes higher-order dependencies. It was originally shown by McKeown et al. [16] that ICA enables powerful exploratory analysis on fMRI data by extracting spatially independent patterns or maps of both task-related activations and artifactual components. Unlike univariate analytic methods, the most prominent feature of ICA as applied to fMRI analysis is that voxels or brain regions are automatically correlated. The problem of how to select the maps of physiological interest out of numerous statistically independent patterns must, however, still be addressed in each experiment. As a solution to this issue, a hybrid technique of ICA and sequential epoch analysis, termed ICS analysis [9,10], was introduced.

Owing to the immensity of the data set, ICS analysis imposes as heavy a computational load as do other
The fixed-point algorithm yield a fast and stable convergence. A class of neural algorithms for the stochastic gradient descent approach does have the advantage of adaptation in a nonstationary system. Adaptability is, however, an unnecessary property for the current fMRI analyses. This tailored ICA algorithm, referred to here as fast ICS, is found to be highly suitable for analysis of high-field fMRI time series by investigating a class of contrast functions based on classical higher-order cumulant measures. The fixed-point iteration is launched from an optimal point derived from a specified temporal pattern and then conducted to converge efficiently on the significant components of sufficient accuracy by employing the optimal contrast [17,18].

In this study, we successfully mapped multiple speech-related areas within the primary motor cortex. The asymmetric clustering on M1p and M1v indicates that phonation and vocalization contribute to hemispheric specialization. On the other hand, the cluster related to silent articulation, M1t, was symmetrically distributed between left and right M1. This symmetry could be interpreted as a bi-hemispheric pattern of innervation of the bulbar musculature responsible for tongue motion. Further analysis of these maps revealed spatially discrete functional clusters on the dominant side. The distances between respective superior and inferior clusters of M1p and M1v (Fig. 5) were significantly larger than the distance between the mean coordinates of the foot and fist region of 22 mm [13], providing further confirmatory evidence that the observed clusters have functional independence within the homunculus of the primary motor cortex. Other smaller clusters of activation were identified, the functional significance of which awaits future studies.

The current study provides direct evidence that human primary motor cortex possesses clear-cut hemispheric specialization similar to that observed for the higher-order cortices. The observed asymmetry in cortical organization of components of speech indicates a differential role of the left and right primary motor cortices in speech production. Greater functional specialization in the left hemisphere, as evidenced by more segregated mapping, suggests a ‘dominant’ role of the left primary motor cortex in speech production. The findings provide a new window to our understanding of the neural mechanisms of normal speech production and can be expected to help lay the groundwork for an improved understanding of motor speech disorders and for devising strategies for speech therapy.

**Table 1** Mean coordinates and distance from cluster center correspond to the standard atlas of MNI template in each cluster

<table>
<thead>
<tr>
<th>Side</th>
<th>Cluster</th>
<th>Number of components</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>Mean distance from cluster center (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left</td>
<td>M1v-s</td>
<td>22</td>
<td>-52 ± 3.5</td>
<td>-11 ± 3.8</td>
<td>47 ± 5.0</td>
<td>3.7 ± 1.6</td>
</tr>
<tr>
<td>Left</td>
<td>M1v-i</td>
<td>11</td>
<td>-54 ± 3.4</td>
<td>0 ± 5.3</td>
<td>23 ± 5.1</td>
<td>4.2 ± 1.7</td>
</tr>
<tr>
<td>Right</td>
<td>M1v</td>
<td>27</td>
<td>58 ± 6.6</td>
<td>-60 ± 5.7</td>
<td>35 ± 8.9</td>
<td>6.7 ± 2.3</td>
</tr>
<tr>
<td>Left</td>
<td>M1p-s</td>
<td>23</td>
<td>-40 ± 5.7</td>
<td>-19 ± 4.0</td>
<td>42 ± 3.3</td>
<td>3.8 ± 2.2</td>
</tr>
<tr>
<td>Left</td>
<td>M1p-i</td>
<td>10</td>
<td>-56 ± 3.7</td>
<td>-2.8 ± 4.2</td>
<td>21 ± 4.1</td>
<td>3.5 ± 1.5</td>
</tr>
<tr>
<td>Right</td>
<td>M1p</td>
<td>30</td>
<td>51 ± 8.3</td>
<td>-11 ± 9.0</td>
<td>38 ± 10</td>
<td>8.5 ± 3.3</td>
</tr>
<tr>
<td>Left</td>
<td>M1t</td>
<td>35</td>
<td>-55 ± 5.1</td>
<td>-80 ± 4.8</td>
<td>32 ± 8.4</td>
<td>11 ± 3.8</td>
</tr>
<tr>
<td>Right</td>
<td>M1t</td>
<td>34</td>
<td>59 ± 5.1</td>
<td>-5.5 ± 4.8</td>
<td>30 ± 8.5</td>
<td>98 ± 4.7</td>
</tr>
</tbody>
</table>

M1v-s and M1v-i represent superior M1v and inferior M1v, respectively. MNI, Montreal Neurologic Institute.

Fig. 5 Schematic of clusters in left M1. Euclidian distances between the mean coordinates of two respective clusters, inferior and superior, were found to be 31 and 26 mm for M1p and M1v, respectively.

ICA-based analyses. To mitigate against this, we formulated a direct exploratory method [10] using a fixed-point ICA algorithm [17]. The algorithm realizes a fast and reliable one-unit search by combining information-theoretic indices with the projection pursuit approach. This direct search technique represents a unique application of ICA in which prior knowledge of mixing weights, or temporal patterns, of desired components is used to control the pursuit direction. In contrast to adaptive neural algorithms, calculations in the fixed-point iteration algorithm are made in batch mode. In other words, a large number of data points, indeed the entire data set if possible, are used in each step of the iteration. In addition, while the fixed-point algorithm has no arbitrary constants such as a learning rate, the convergence of general neural network algorithms depends strongly on a deliberate choice of the learning rate, which even if the value were optimal, still yields a convergence speed that is much slower than the proposed algorithm. These features of
Conclusion

Human primary motor cortex possesses clear-cut hemispheric specialization similar to that observed for the higher-order cortices. ICS analysis of high-field fMRI time series demonstrated that, within the dominant hemisphere, spatially and functionally independent components corresponding to phonation and verbalization formed distinct clusters. Greater functional specialization of the primary motor cortex in the dominant hemisphere indicates its predominant role over that of the nondominant hemisphere for speech production.

References