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Functional brain laterality for sequential movements: Impact of transient practice

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Abstract **The impact of learning on brain functional laterality has not been systematically investigated. We employed an event-related functional magnetic resonance imaging combined with a delayed sequential movement task to investigate brain activation pattern and laterality during a transient practice in 12 subjects. Both hemispheres, involving motor areas and posterior parietal cortex, were engaged during motor preparation and execution, with larger activation volume in the left hemisphere than in the right. Activation volume in these regions significantly decreased after a transient practice, with more reduction in the right hemisphere resulting increase in left lateralization. The theoretical implications of these findings are discussed in relation to the physiological significance of brain functional laterality.**

The laterality of brain function is one of fundamental questions in the field of neuroscience. Traditional view holds that language processing primarily depends on the left cerebral hemisphere, whereas processing of spatial information is mainly associated with the right hemisphere. This view has been challenged by more recent studies, which suggest the involvement of both hemispheres in language as well as spatial processing. Until most recently, voluntary movement of unilateral limb was believed to be controlled solely by contralateral hemisphere. However, neuroimaging studies of this group and others have demonstrated that ipsilateral hemisphere also plays important roles in various movement tasks[1—5].

The origin and physiological significance of functional hemispheric laterality remain poorly understood. It has been widely accepted that the functional brain laterality results from evolutionary, developmental and experiential factors. However, empirical data for the impact of experience, including learning, are sparse. While several

studies did observe functional brain lateralization along with long-term learning[6,7], the effect of short-term learning has not yet been systematically investigated. It has been shown that short-term learning can increase effectiveness of information processing, and information transfer within a hemisphere appears to be more effective than inter-hemispheric communications[8]. Therefore, we hypothesize that even transient practice could increase functional laterality.

Traditional research techniques, including dichotic listening, Wada test, neuropsychological assessment of split-brain patients, can only provide behavioral measures and are unable to look insight into brain activities. In the present study, event-related functional MRI was used to directly examine changes of brain activity during learning processing, in order to provide empirical data for further understanding the physiological significance of this phenomenon.

1 Materials and methods

( ) Subjects.   Twelve healthy volunteers (9 males, 3 females), ages 18—23, served as subjects. All were right-handed as determined by a Chinese version of a standardized inventory [9]. None had any history of psychiatric and neurological problems.

( ) Motor task.   We employed an event-related functional magnetic resonance imaging combined with a delayed sequential movement task to investigate brain activation associated with motor preparation and execution respectively[10,11]. A trial began with a CUE signal, which provided a random sequence for movement. The subjects were asked to remember the sequence and to make a movement. After a delay of 14 s, an imperative GO signal was presented and the subject tapped the fingers (except the thumb) of the right hand as quickly as possible according to the prepared sequence. Each finger moved once in the each trial. There were 9 trials in each run, which lasted 4 min and 20 s. Three runs were conducted for each subject and activation during the first and third runs was examined.

( ) MRI equipments and scanning parameters.   A 1.5 GE magnetic resonance imaging system was used. The following 3 types of images were collected in all subjects[2,10].

Two-dimensional anatomical images.   T1-weighted spin echo sequence (axial, TR/TE = 380/9 ms, Slice thickness = 5 mm, Skip = 0 mm, Slices number = 7, FOV = 240 mm × 240 mm, matrix = 256 × 256) was used to acquire 2-D anatomical data.

Functional images.   A T2*-weighted gradient-echo echo planar sequence was used for fMRI scans (TR/TE= 2000/50 ms, Flip Angle = 90°, matrix = 64 × 64) at the same positions of 2-D anatomical images. For each slice, 126 images were acquired with a total scan time of 260 s

in a single run.

Three-dimensional whole-brain anatomical images. 124 contiguous T1-weitghted sagittal images, covering the whole brain volume, were collected with a spoiled gradient-recalled at steady-state (SPGR) sequence (TR/TE = 30/6 ms, Flip Angle = 35°, thickness = 1.3 mm, FOV = 240 mm × 240 mm, matrix = 256 × 256).

( ) Data analysis.   Analysis of data, only briefly described here, was similar to that reported in our previous study[12]. First, functional images were preprocessed, including motion correction, spatial normalization, and spatial smoothing (with an isotropic Gaussian kernel of full width at half-maximum (FWHM) 5 mm). Impulse response function (IRF) of each voxel was then estimated by deconvolve algorithms and IRF was convolved with the function of stimuli. Finally, multiple linear regression analysis was used to calculate the fitness between the estimated model and the observed data, and F value of each voxel was obtained. Only those voxels whose F value equaled or was larger than 19 $(P < 1.4 \times 10^{-15})$ were considered as active and superimposed on the normalized 3-dimensional whole-brain anatomic images to produce statistical parametric maps of preparation and execution respectively. P values of activated voxels were coded by pseudo-colors.

Activation volumes in each hemisphere were measured under the following conditions: preparation before and after learning, and execution before and after learning. Laterality index (LI) was calculated under each condition as follows: LI = (left − right)/(left + right), where left is the number of activated voxels in the left hemisphere and right in the right hemisphere[13]. The value of LI ranges from −1 to +1, with a negative value indicating right hemispheric dominance and a positive value indicating left hemispheric dominance.

2 Results

Figure 1 shows average activation maps of 12 subjects for motor preparation and execution before (the first run) and after (the third run) learning. Before learning (Fig. 1, upper panels), the secondary motor areas, such as bilateral anterior supplementary motor area (SMA), premotor cortex (PMC) and posterior parietal cortex (PPC), were significantly activated during motor preparation, while primary motor cortex (M1), bilateral PMC and anterior part of PPC were activated during motor execution (Fig. 1, lower panels). Activation volume in the left hemisphere was larger than that in the right in both tasks. However, in individual level, this was true in only 8 out of 12 subjects during preparation, and 11 out of 12 during execution. Although essentially same brain areas were activated before and after learning, during motor preparation as well as during motor execution, activation volumes in both hemispheres significantly decreased after learning, with more reduction in right hemisphere (for preparation: the
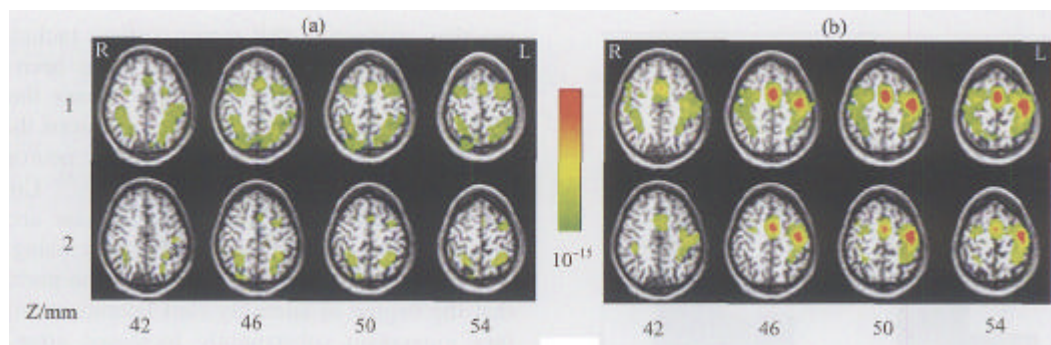
Fig. 1. Averaged activation maps for a delayed sequential motor task before and after learning. (a) Motor preparation; (b) motor execution. Note that areas activated before learning (upper panels) were larger than those after learning (lower panel) for both tasks. *P* value is coded with pseudo-color. Z is the distance (mm) from the slice shown to the zero panel in the standard coordinates defined by Talairach and Tournoux atlas. 1: before learning; 2: after learning.

decrease rates of left and right hemispheres were 23% and 45% respectively, and the difference was statistically significant, *P*<0.05. For execution: the decrease rates of left and right hemispheres were 19% and 41% respectively, *P* < 0.05).

We then performed 2(before and after learning)×2 (left and right hemisphere) analysis of variance (ANOVA) with repeated measure for the activation volume (number of activated voxels) during preparation and execution respectively (Fig. 2). Because data before and after learning were obtained from all subjects studied, the learning variable was treated as repeated measure factor to increase statistical power. During motor preparation, activation volume after learning was smaller than that before learning (*P* < 0.05), with larger activation volume in the left hemisphere than in the right both before and after learning (*P* < 0.01). During motor execution, the mean activation volume after learning was also smaller than that before learning, but the difference was not significant (*P* = 0.11). Similarly, activation volume for execution in the left hemisphere was larger than in the right hemisphere either before or after learning (*P* < 0.01). The interaction between learning and hemisphere was not significant (*P* > 0.05).

LIs during preparation and execution before and after learning are shown in Fig. 3. Single sample *t*-tests showed that LIs in all conditions were not equal to zero. Before learning, LI for preparation was 0.14 ± 0.18 (significantly larger than 0, *P* < 0.02) and 0.18 ± 0.17 (*P* < 0.004) for execution. After learning, LI changed to 0.35 ± 0.29 (*P* < 0.001) for preparation and 0.42 ± 0.30 (*P* <0.001) for execution. The differences of LI before and after learning were then compared using paired-sample *t*-test, and LI significantly increased after learning for both tasks (for preparation: *P* < 0.003; for execution: *P* < 0.001).

3 Discussion

Brain activations during movement preparation and execution were characterized using event-related fMRI combined with a delayed sequential finger movement task, and activation volume and laterality indices before and after a transient practice were quantitatively analyzed.

The results showed that the secondary motor areas such as anterior SMA, PMC, and PPC were engaged during motor preparation, whereas M1, bilateral PMC, and anterior part of PPC were activated during motor execution. Toni and his colleagues[14] conducted the first study to identify the brain structures associated with motor preparation and execution by use of event-related fMRI and a delayed motor task. They found that PMC, PPC, and
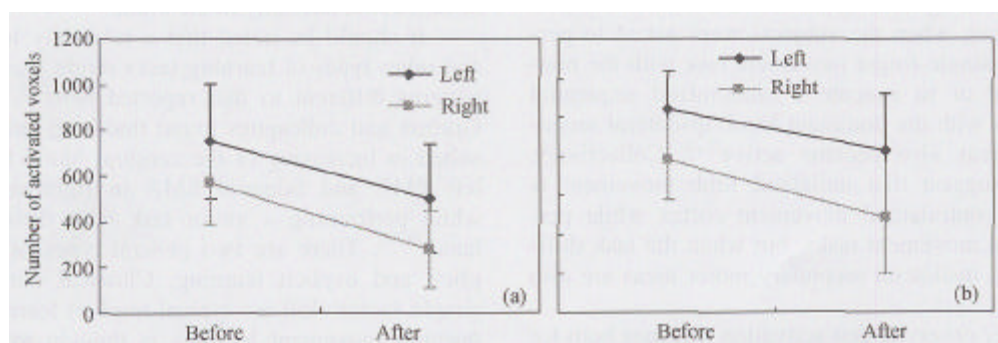

Fig. 2. Activation volume (M± SD) (shown as the number of voxels, 27 mm³ per voxel) in the left and right hemisphere during motor preparation (left) and execution (right) before and after learning. (a) Motor preparation; (b) motor execution.
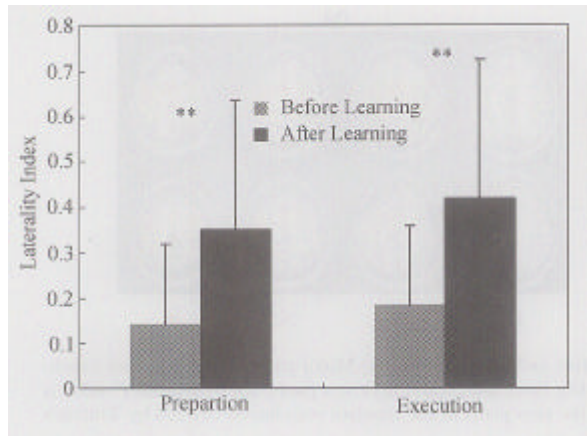
Fig. 3. Laterality Index (M± SD) for motor preparation and execution before and after learning. ** indicates $P < 0.001$, before vs. after learning.

SMA were mainly involved in motor preparation, whereas M1 was activated during motor execution. In contrary to the present study, Toni and associates failed to detect significant activation in PMC and anterior part of PPC during movement execution, nor did they describe the function of anterior SMA[14]. This discrepancy is possibly due to methodological difference in that they employed a single-finger movement task, a much simpler task than that used in the present study. Indeed, using the sequential movement task, a paradigm similar to ours, Hanakawa et al.[15] reported activation pattern almost identical to that found in the current study, although movement imagination rather than preparation was engaged in their experiment.

An interesting finding of the present study is that both sides of cerebral cortex were significantly activated either during motor preparation or during execution and only slightly left lateralization was found. This finding suggests that sequential movement is not exclusively controlled by the contralateral hemisphere. At the first look, this result seems to conflict with the traditional view, but they can be easily reconciled. Our previous study showed that activation was confined to contralateral PMC and SMA in a single-finger movement task with the dominant hand[1]. However, when the subjects were asked to perform the same single-finger movement task with the non-dominant hand or to execute a randomized sequential movement task with the dominant hand, ipsilateral secondary motor areas also became active[1,2]. Collectively, these results suggest that unilateral limb movement is controlled by contralateral movement cortex while performing simple movement tasks, but when the task difficulty increases, ipsilateral secondary motor areas are also recruited[4].

We further observed that activation volumes both for motor preparation and execution in all regions activated before learning significantly reduced after a transient

practice, suggesting that motor cortices including M1 are engaged in learning process[16,17]. It has been well documented that transient practice can enhance the selectivity of neuronal populations: only those neurons that represent the stimuli become active, while other neurons that less relevant to the stimuli are inhibited[17,18]. Consequently, the number of activated neurons decrease and activation volume reduces along with learning processing.

The most interesting finding of the present study is that the degree of laterality (left lateralization) for voluntary movement substantially increased after a transient practice of merely several minutes. Although enhancement of lateralization induced by learning has been reported both in humans and animals, quantitative analysis of the difference between two hemispheres and observation of transient practice have been lacking[6,19—21]. Subsequent analyses of changes in activation volume and the change rates of two hemispheres indicated that the increased left lateralization was resulted from more reduction in the right hemisphere (ipsilateral hemisphere of movement limb). These findings, combined with our previous studies using single-finger and sequential motor tasks, suggest that laterality of brain function may be related to task difficulty. Before learning, the task is relatively difficult, thus depending on bilateral brain areas. After learning, task difficulty decreases and unilateral brain area can accomplish the task, thus less depending on the other side of the brain. The impact of learning and evolutionary on laterality therefore appears to share many common mechanisms: both can be regarded as the process of reorganization and optimization of the utility of brain resources. Functional lateralization can increase effectiveness of information transfer and reduce the competition and interference between hemispheres[8]. On the other hand, if a task is more difficult, it has to depend on the cooperation of two hemispheres, though at the cost of time and efficiency of processing. Although further study is needed to verify this hypothesis, the present study provided preliminary data that would be helpful to refine our understanding of physiological significance and the origin of functional laterality in the brain.

It should be noted that a relatively longer practice and other types of learning tasks might lead to activation patterns different to that reported here[22]. For example, Grafton and colleagues found that long-term learning resulted in increasing of the cerebral blood flow (CBF) in left PMC and bilateral SMA in right-handed subjects while performing a motor task with their left or right hand[19,20]. There are two general types of learning, implicit and explicit learning. Classical conditioning and simple motor skill are typical implicit learning, while sequential movement learning is thought to be related to both types of learning. In the early stage, implicit learning is dominant; in the late stage, explicit learning plays a

more important role because the subjects become aware of the goal of the learning task along with practice[23]. It has been shown that during classical conditioning, CBF significantly decreased in the right cerebellum, right prefrontal areas, right parietal cortex, and insula, but increased in a number of the left cortical areas[6]. Taken together, although learning shows the same trend, i.e., increased laterality, across different types of learning with different durations of practice, the regional changes of brain activity are greatly variable. Accordingly, further study is needed to investigate to what degree the difference is related to type and duration of learning, and number of practice trial. Furthermore, the current study only examined the impact of transient practice on functional laterality in the whole brain level, lateralization in individual brain regions are under investigation.

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