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Original Article

Reorganization of Cortical Language Areas in Patients with Aphasia: A Functional MRI Study

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The purpose of this study is to delineate the pattern of reorganization of cortical language areas using functional magnetic resonance imaging (fMRI) after rehabilitation therapy in patients with aphasia. Six right-handed aphasic patients were investigated. Causes of aphasia were intracerebral hemorrhages of the left basal ganglia in 3 patients, cerebral infarction of the left MCA in 2, and surgical resection of the frontotemporal lobes to control intractable epilepsy in 1. An auditory sentence completion task was used to activate brain language areas during the fMRI. Three patients with left frontal lesions showed activation in the right inferior frontal lobes while performing language tasks, whereas the other 3, whose lesions located at subcortical areas, showed activation in the bilateral frontal and temporal lobes. Our results demonstrated the differences in interhemispheric reorganization of the language network depending on the location of the lesion in aphasic patients. While the patients with subcortical lesion showed tendency of bilateral frontal activation, those with cortical lesion showed activation of the right frontal lobe.

Key Words: Aphasia, language area, reorganization, functional MRI

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INTRODUCTION

Evidence for the capacity of patients with brain injuries to demonstrate continuing recovery for years after sustaining their injury has existed for a long time. The mechanism of this recovery is based on the plasticity of the brain which is considered to be significant in the language area. Reorganization of intra- and/or interhemispheric language networks is thought to occur in patients who have recovered from aphasia. Most individuals with aphasia show some recovery of language function, despite persisting damage to the left hemispheric language areas.[1] The greatest improvement has been shown to occur within the first 6 months following onset, particularly the first 3 months.[2] Late recovery, however, for several years beyond the initial recovery period, and even after 5 - 10 years, has been reported.[3] No research has been reported about the relationship between recovery patterns and lesion sites.

A number of methods, such as SPECT, PET, and functional MRI (fMRI), have been used to visualize the change and reorganization of neural networks during stroke recovery. FMRI is increasingly being used because of its superior time resolution and finer spatial resolution. The technique is non-invasive without radiation hazards, which allows for longitudinal studies within the same individual.

The purpose of this study was to delineate the pattern of reorganization in the language areas after rehabilitation therapy in patients with aphasia using fMRI and to determine if there are any differences in these patterns between the patients with cortical or subcortical brain lesions.

MATERIALS AND METHODS

Six right-handed aphasic patients (5 male, 1 female) were studied. The mean age was 47.2 ± 9.3 years (range: 31 - 58 years) and the mean modified Edinburgh score of prestroke status was +100.0. The 3 patients with lesions in the left frontotemporal area, two due to cerebral infarction and one surgical resection for controlling epilepsy initially showed the clinical pattern of global aphasia. However, the pattern was converted to motor aphasia at the second evaluation because their language comprehension ability was improved after treatment. The other 3 patients had lesions in the left basal ganglia due to intracerebral hemorrhage and presented with motor aphasia at both initial and follow-up assessments, even though their overall language abilities were improved. All subjects gave informed consents. The study protocol was approved by the Institutional Review Board at Chonbuk National University.

The type and severity of aphasia were evaluated initially (score 1) and at the time of fMRI (score 2) using a Chonbuk University aphasia test battery (CBATB) and the Korean version of the Boston Naming Test. The initial evaluation was performed within 1 month after stroke, and the second evaluation was performed at the time of fMRI. The mean time to the fMRI experiment was 14.8 months (3 to 30 months) after stroke. CBATB consisted of 37 test items to assess oral expression ability, auditory comprehension, reading comprehension, oral reading, writing and naming. Performance was measured by the percentage of correct responses. The mean language score at the initial evaluation was 36.5 ± 22.4%, which improved to 66.6 ± 16.1% at the time of fMRI scanning. All patients showed remarkable improvement at the time of fMRI compared to the initial state (Table 1).

A sentence completion task was implemented with a block design in order to assess the language areas during the fMRI experiment. Subject and auxiliary words were given through headphones and patients were instructed to silently generate the related verb and complete the sentence. White noise was given as a control task. The duration of each block was 38.4 seconds and the active/control pair was repeated 4 times. The fMRI task paradigm was designed using Superlab Pro 2.0 software (Cedrus Co., Phoenix, AZ, USA).

Table 1. Subject Characteristics

Patient	Age (yr)	Sex	Brain lesion	Type of aphasia	Time from stroke to fMRI	Language score 1 (%)	Language score 2 (%)	Modified Edinburgh score
1	53	Female	Lt. MCA* infarction	Global	3 mo	17.8	48.4	100
2	47	Male	Lt. MCA* infarction	Global	21 mo	17.5	63.7	100
3	44	Male	Lt. frontotemporal lobectomy	Global	19 mo	42.7	72.2	100
4	50	Male	Lt. basal ganglia HICH†	Motor	13 mo	16.3	48.1	100
5	58	Male	Lt. basal ganglia HICH†	Motor	3 mo	65.8	83.1	100
6	31	Male	Lt. basal ganglia HICH†	Motor	30 mo	58.8	84.3	100
Mean SD	47.2 ± 9.3				14.8 ± 10.7	36.5 ± 22.4	66.6 ± 16.1	100

*Middle cerebral artery.
†Hypertensive intracerebral hemorrhage.

All subjects were imaged using a 1.5T Siemens Vision scanner. Twenty slices were acquired using single shot EPI sequences (TR/TE=3840/40 ms, Flip angle 90°, FOV 220 mm, 64 × 64 matrix, slice thickness 6 mm). In all functional runs, the MR signal was allowed to achieve equilibrium over the first four scans that were excluded from analysis. This produced 80 experimental scans (10 active/control; repeated 4 times) from the 84 images of each functional run. T1 or T2 weighted anatomic images were acquired in the transaxial planes parallel to the AC-PC line for use as the anatomic overlay.

The fMRI data was analyzed using SPM-99 software (Wellcome Department of Cognitive Neurology, London, UK) run under the MATLAB environment (The Mathworks Inc., Natick, Ma, USA). All functional images were realigned and then coregistered to the anatomic images. The images were smoothed using an 8 mm isotropic Gaussian kernel. The functional data from each individual subject was statistically analyzed using analysis of covariance (ANCOVA). Statistical parametric maps were obtained and voxels were considered significant if their Z scores were significant at a threshold of $p < 0.001$ uncorrected.

RESULTS

Brain activation areas in aphasic patients with cortical lesions

Patient 1

The primary brain lesion of this patient was in the left frontotemporal lobe as a result of MCA infarction. The fMRI results of the auditory sentence completion task showed activation in the right middle and inferior frontal areas, which are represented by the Broca homologue area. Small activation in the left frontal area adjacent to the lesion was also seen (Fig. 1-A).

Patient 2

The primary brain lesion was in the left frontotemporal lobe as a result of MCA infarction. The fMRI study showed activation in the right middle frontal lobe. Small activation was also seen in left middle frontal lobe adjacent to the lesion (Fig. 1-A).

Patient 3

The primary brain lesion was an extensive resection of the left frontotemporal lobe to control intractable epilepsy. The fMRI study showed main activation only in the right inferior frontal lobe. No activation was seen in the left frontal region (Fig. 1-A).

Brain activation areas in aphasic patients with subcortical lesions

Patient 4

The primary brain lesion was a left basal ganglia hemorrhage. The fMRI results showed activation in the bilateral inferior frontal and superior temporal lobes. Additional activation was seen in the right basal ganglia. The activation was more extensive in the right frontal lobe than the left hemisphere (Fig. 1-B).

Patient 5

The primary brain lesion was a left basal ganglia hemorrhage. The fMRI results showed activation in the bilateral inferior frontal and superior temporal lobes. Additional activation was seen in the right basal ganglia. Temporal and frontal activations were more extensive in the left hemisphere (Fig. 1-B).

Patient 6

The primary brain lesion was a left basal ganglia hemorrhage. The fMRI results of the auditory sentence completion task showed activation in the bilateral frontal and temporal lobes and the right basal ganglia. Activation of left the hemisphere was more prominent than the right hemisphere (Fig. 1-B).

DISCUSSION

The recovery of function following brain damage has been extensively researched. Brain plasticity can be considered as a major factor in recovery but its mechanisms are varied.[4,5] The role of the non-stroke containing hemisphere in language recovery was recently studied using

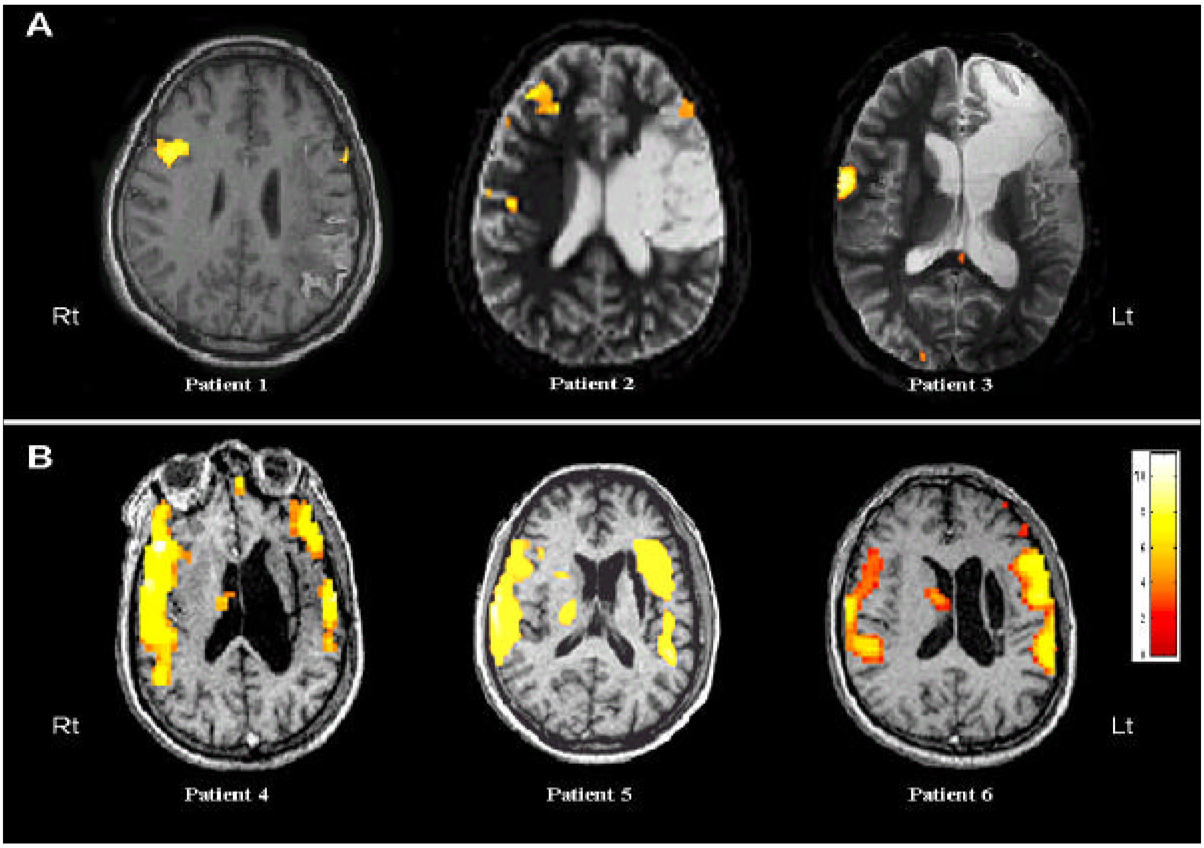

Fig. 1. (A) Activation areas were superimposed on the T1 (patient 1) and T2 (patients 2 and 3) weighted anatomic images. Lesions were located in the left frontotemporal lobes due to MCA infarction in patients 1 and 2, and a surgical resection in patient 3. Significant activation can be seen in the right frontal lobes in all cases. Small activation foci are seen in the perilesional areas in patients 1 and 2. (B) Activation was superimposed on the T1 weighted anatomic images. Bilateral frontal and temporal activation, as well as activation of the right basal ganglia, are seen in all cases (patients 4, 5 and 6).

functional neuroimaging methods. Cappa et al. studied the recovery patterns after stroke in acute aphasic patients using PET.[6] Eight patients with unilateral left hemispheric stroke were investigated, subsequent to the stroke and 6 months later with results suggesting that language recovery in the first month after onset was associated with the regression of functional depression (diaschisis) in structurally unaffected regions, particularly in the right hemisphere. Mimura et al. used SPECT to performed a study of 20 aphasic patients within the first year of their stroke and 16 aphasic patients 7 years after their stroke.[7] They concluded that the initial language recovery was primarily associated with activation of the dominant hemisphere and long-term recovery with activation of the contralateral hemisphere, especially in the homotopic frontal and thalamic areas. Karbe et al. reported that activation of the left supplementary motor area was the most prominent compensatory area in the subacute stage of post-stroke aphasic patients using PET.[8] They also commented that compensatory activation of the right hemisphere was related with poor prognosis, while repair of the left hemispheric language network was a hallmark of functional recovery. On the other hand, Musso et al reported that activation of the right posterior superior temporal gyrus and the left precuneus were best correlated with improvement in verbal comprehension.[9] A recent fMRI study by Thulborn et al demonstrated the spontaneous redistribution of function to the right hemisphere that occurred within days and continued over months as performance returned to normal during the recovery from aphasia.[10] Thulborn also mentioned other compensatory cortical activations such as the areas directly adjacent to the lesions.

Our study confirms the importance of the right hemispheric contribution to the functional recovery of aphasic patients. However, the pattern of right hemispheric activation was dependent on the location of the brain lesion. Our results demonstrated that aphasic patients with cortical lesions showed fMRI activation in the contralateral frontal areas. This can be interpreted to indicate that the interhemispheric shift of the cortical language network is the main mechanism of recovery in these patients. On the other hand, aphasic patients with subcortical lesions showed activation in the bilateral frontal lobes and in the right subcortical area. These findings suggested that the interhemispheric reorganization of the language network was accomplished not only at the level of the cerebral cortex, but also at the level of the subcortical feedback system. The final language outcome, as assessed by CBATB, was slightly greater in this subcortical group than in the cortical lesion group. In our study, two patients showed activation of right frontal lobes at 3 months following the onset of stroke. This early interhemispheric redistribution of blood flow was congruent with the results of Thulborn's study.[10] Early language intervention may influence this early blood flow shift and associated functional reorganization of the language network.

The limitations of this study were an irregular imaging interval from the onset of disease to fMRI scanning and a lack of follow-up fMRI results. Follow-up fMRI would be very helpful in detecting the changes of the reorganization patterns according to the stages of recovery after a brain injury. Many studies have demonstrated that the rehabilitation therapy improves functional brain reorganization.[9,11-13] The effects of successful rehabilitation in the reorganization of the language network could be visualized by serial fMRI in patients with aphasia.

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