Near-Infrared Spectroscopic Topography as a Tool to Monitor Motor Reorganization After Hemiparetic Stroke

A Comparison With Functional MRI

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Background and Purpose—Motor functional recovery from stroke can occur, but the mechanisms underlying this restorative process remain to be elucidated. We used near-infrared spectroscopic (NIRS) topography in comparison with functional MRI (fMRI) to evaluate the compensatory motor activation of cortical regions in patients who recovered from hemiparesis after cortical cerebral infarction.

Methods—We examined 6 right-handed patients who suffered cerebral infarction of the middle cerebral artery territory with minimal or mild residual contralateral hemiparesis (4 men and 2 women, 59 to 79 years old, all had left hemiparesis). Both fMRI and NIRS were studied during a hand movement task at chronic stages. Five right-handed, normal subjects (3 men and 2 women, 44 to 81 years old) served as controls.

Results—fMRI and NIRS detected very similar cerebral cortical activation, although NIRS detected only superficial activation. The spatial resolution of NIRS was less than that of fMRI, but NIRS provided a dynamic profile of activation. Normal subjects activated predominantly the contralateral primary sensorimotor cortex and supplementary motor areas during each hand movement. All the stroke patients exhibited the normal activation pattern during normal hand movement. On affected hand movement, the stroke patients showed extended activation not only in the contralateral motor cortex but also in the ipsilateral motor cortex (primary motor cortex and supplementary motor areas).

Conclusions—Both fMRI and NIRS studies provided evidence for the contribution of ipsilateral motor cortical compensation or reorganization to the recovery from poststroke hemiparesis. The result demonstrated that NIRS was a unique tool to monitor poststroke alterations in cortical motor functions. (Stroke. 2002;33:2032-2036.)

Key Words: cerebral infarction ■ magnetic resonance imaging ■ neuronal plasticity ■ paresis ■ spectroscopy, near-infrared

Hemiparesis is the most common neurological deficit after stroke and is one of the most critical determinants of functional prognosis.1 There is a wide range of recovery of hemiparesis after stroke, and complete recovery of motor function is not exceptional.2 However, the mechanisms and determinants of this restorative process have been incompletely understood. Recent studies have suggested that the recovery of motor function after stroke is facilitated by the recruitment or reorganization of the cortical motor function in both damaged and nondamaged hemispheres. Accumulation of such evidence depended on the development of new techniques for the study of the physiology and pathophysiology of motor function, such as positron emission tomography (PET),3,4 transcranial magnetic stimulation,5-7 and functional MRI (fMRI).8,9

Another recent technique is near-infrared spectroscopic (NIRS) or optical topography.10 NIRS topography is a noninvasive approach for continuous monitoring of the amounts of oxygenated hemoglobin (oxy-Hb) and deoxygenated Hb (deoxy-Hb),11 which are closely correlated to the neural activity of the brain. NIRS topography provides only 2D brain surface mapping with limited spatial resolution but offers the advantage of high temporal resolution and resistance to motion artifact, enabling the measurement to be performed in a recumbent or sitting position. This method has been shown to reflect cerebral cortical activation related to motor activity,12,13 mental tasks,14 visual and auditory stimulation,15,16 speech,17 and epileptic seizures.18 Until now, no complete study of poststroke motor recovery with NIRS has been reported. Therefore, we examined 6 patients who suffered cortical cerebral infarction of the middle cerebral artery (MCA) territory and recovered without severe contralateral hemiparesis. In this study, we used both fMRI and NIRS topography in the same patients to study poststroke alterations in motor activation of cortical regions and compared the efficacy of the 2 techniques.
Materials and Methods

Subjects
Six patients (mean 72 years old; range 59 to 79 years; 4 men and 2 women) with a cortical cerebral infarct of the MCA territory without severe hemiparesis were identified from review of records of our hospital (Table 1). All of them were right-handed. The time between the onset of stroke and the examination ranged from 2 months to 8 years. All the infarcts were evidenced by MRI and were located in the right hemisphere, involving more than half of the MCA territory. All the patients had left hemiparesis of various degrees, ranging from mild to severe at the onset of stroke, and then recovered to levels of minimal or mild hemiparesis. Their activities of daily living were mild to severe at the onset of stroke, and then recovered to levels of minimal or mild hemiparesis. Their activities of daily living were independent when examined (0 to 2 of the modified Rankin scale). Five right-handed, normal subjects (mean 64 years old; range, 44 to 81 years; 3 men and 2 women) served as controls.

Functional MRI
Functional MRI studies were performed with a 1.5 T Siemens Magnetom Symphony scanner. Blood oxygenation level-dependent images were obtained continuously in a transverse orientation with a gradient-echo, single-shot echo-planar imaging pulse sequence. The acquisition parameters were as follows: repetition time 3 s, time of echo 62 ms, flip angle 90°, 3-mm slice thickness, 15 slices through the supratentorial brain, field of view 192×192 mm, and 128×128 matrix.

During the fMRI scan, the patients and normal controls performed a sequential, self-paced hand grasping task (sequential flexion and extension of all fingers). This task performance occurred in periods of 30 s, interspaced with 30-s rest periods. The cycle of task and rest was repeated 5 or 6 times during each hand movement. A staff member monitored the patients directly throughout the study, and gave the start and stop signals by tapping gently on the knee. Absence of mirror movements was confirmed.

Data analysis was performed with Statistical Parametric Mapping 99 (Wellcome Department of Cognitive Neurology, London, UK; http://www.filion.ucl.ac.uk/spm/) implemented in MATLAB (The MathWorks Inc). The first 5 images of each run were discarded to allow signal stabilization, and the remaining 100 or 120 volumes of 15 slices were used for analysis. After smoothing, the general linear model was used for the detection of activated voxels. If large movements of the head occurred, the data were discarded. Usually, the voxels were considered as significant if $P < 0.01$ (corrected for multiple comparison). The activation images were overlaid on T1-weighted anatomic images.

NIRS Topography
NIRS measurements were performed using a 24-channel optical topography system (Advanced Research Laboratory, Hitachi Ltd) during 6 cycles of 15-s hand grasping and 45-s rest while sitting on a reclining chair. Twenty-four channels (12 channels on each side) were mounted on head shells (60×60 mm each) and placed on the scalp overlaying both sensorimotor cortices. Near-infrared light with wavelengths of 780 nm and 830 nm was guided by optical fiber bundles (2 mm in diameter) and transmitted into the cranium. The reflection of the infrared light was sampled by receiving probes placed on the scalp 30 mm away from the transmitting probe and was detected with silicon photodiodes. The infrared light was absorbed predominantly by the brain tissue hemoglobin mainly at approximately 20 mm below the scalp. The near-infrared light intensity was modulated at different frequencies to prevent cross-talk between the channels and the wavelengths. The changes in the oxy-Hb and deoxy-Hb concentrations were calculated using the difference in the absorption indexes for the 2 wavelengths. Total Hb was defined as the sum of oxy-Hb and deoxy-Hb. The magnitude of changes in oxy-Hb, deoxy-Hb, and total Hb was displayed as a contour map (NIRS topography). As a result, 12 NIR spectrographs and an NIRS topograph were obtained on each hemisphere. The topography can be visualized as dynamic, real-time images, but only representative still NIRs topographs were shown here.

Statistical Analysis
Because the NIRS data were semiquantitative, the activation of the hand motor area on fMRI or NIRS topography during hand movements was graded using a scoring system with 0=no activation, 1=slight activation, 2=moderate activation, and 3=intense activation. Full brain activation observed during hand movements in control subjects was scored as grade 3 and used as a standard. Statistical analysis was performed with the Mann-Whitney U test. Probability values less than 0.05 were considered significant.

Results

Normal Subjects
Normal subjects exhibited activation on fMRI predominantly in the contralateral primary sensorimotor cortex (SMC) and supplementary motor areas (SMA) during each hand movement. Activation in the ipsilateral SMC was observed occasionally but only to a limited extent. There was no difference between the right hand and left hand movements.

NIR spectroscopy and topography also showed predominant activation (an increase in oxy-Hb and a concomitant decrease in deoxy-Hb) in the contralateral SMC during each hand movement. The activation often appeared bilateral, but the ipsilateral activation was to a lesser degree.

Stroke Patients
All the stroke patients exhibited the normal activation pattern during right (normal) hand movement on fMRI (Figure 1). On left (affected) hand movement, the patients showed bilateral activation on fMRI with various extent of ipsilateral primary SMC activation (Figure 1). Four of 6 patients showed enlarged activation in the contralateral parietal cortex or a posterior shift compared with the activation during normal hand movements. Enlarged activation of the SMA during affected hand movement was seen in 3 of 6 patients.

All the patients showed the normal activation pattern during normal hand movements on NIR spectroscopy and topography. The stroke patients exhibited bilateral SMC

### Table 1. Clinical Characteristics of Stroke Patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Location</th>
<th>AF</th>
<th>Time to Scan</th>
<th>Grasping Power (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>59</td>
<td>M</td>
<td>R MCA, total</td>
<td>-</td>
<td>5 yr</td>
<td>R 25/L 6</td>
</tr>
<tr>
<td>2</td>
<td>68</td>
<td>M</td>
<td>R MCA, total</td>
<td>-</td>
<td>8 yr</td>
<td>R 32/L 30</td>
</tr>
<tr>
<td>3</td>
<td>71</td>
<td>M</td>
<td>R MCA, branch</td>
<td>+</td>
<td>2 mo</td>
<td>R 37/L 38</td>
</tr>
<tr>
<td>4</td>
<td>78</td>
<td>F</td>
<td>R MCA, branch</td>
<td>+</td>
<td>2 mo</td>
<td>R 16/L 14</td>
</tr>
<tr>
<td>5</td>
<td>79</td>
<td>M</td>
<td>R MCA, branch</td>
<td>-</td>
<td>7 yr</td>
<td>R 18/L 18</td>
</tr>
<tr>
<td>6</td>
<td>79</td>
<td>F</td>
<td>R MCA, total</td>
<td>+</td>
<td>6 yr</td>
<td>R 20/L 18</td>
</tr>
</tbody>
</table>

MCA indicates middle cerebral artery territory; AF, atrial fibrillation; M, male; F, female.
activation during affected hand movement, and the ipsilateral activation was stronger in 3 of 6 patients (Figure 2). Temporal profile of the activation could be seen as a transient increase in oxy-Hb and a concomitant decrease in deoxy-Hb (Figure 2).

Semiquantitative scoring demonstrated a statistically significant increase in the activation of ipsilateral motor cortex during affected (left) hand movement on both fMRI and NIRS topography (Table 2).

Discussion

In the present study, both fMRI and NIRS were used to evaluate hand movement in patients with minimal or mild residual hemiparesis after ischemic stroke of the MCA territory. In control subjects, hand movement produced brain activation predominantly in the contralateral SMC and SMA on fMRI. This result is consistent with earlier fMRI studies in normal individuals.8,9,20,21 Stroke patients activated not only contralateral SMC and SMA, often to a larger extent than control, but also the SMC ipsilateral to hand movement (unaffected hemisphere). This altered or extended pattern of activation (reorganization) in the contralateral and ipsilateral motor cortices after recovery from stroke are also consistent with previous reports in patients with stroke of various locations.8,9,22 These functional changes in the brain after stroke suggest that reorganization (plasticity) of the cortical network for motor control may contribute to adaptations leading to functional recovery of poststroke hemiparesis.

The findings with NIRS topography, examined in the same patients as fMRI, were in good agreement with the fMRI findings. Because both fMRI and NIRS are based on the tight coupling between neuronal activity and an increase in regional cerebral blood flow, this agreement is reasonable and expected. The spatial resolution of NIRS topography is poor, being approximately 25 mm,23 and only the superficial cerebral cortex 10 to 20 mm below the scalp can be monitored.24 However, the unique advantages of NIRS are continuous, dynamic monitoring and resistance to motion artifacts because the NIRS probes are mounted firmly on the head, thus providing a considerable freedom in the task design, even in infants without sedation. In contrast, the subjects need to be placed in a narrow gantry and have their head fixed during the entire examination with fMRI or PET. An additional merit of NIRS is the availability for patients with metal devices, such as cardiac pacemakers, for whom MRI is contraindicated. Furthermore, NIRS is a compact, portable, and low-cost instrument. Thus, NIRS is a unique tool for monitoring cortical brain function.10 Improvement of the spatial resolution and development of whole brain scanning by increasing the number of the channels would increase the importance of this technique.

Table 2. Activation of the Hand Motor Area During Hand Movement in Normal Controls and Stroke Patients Assessed With fMRI and NIRS Topography

<table>
<thead>
<tr>
<th></th>
<th>fMRI</th>
<th>NIRS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R Hand</td>
<td>L Hand</td>
</tr>
<tr>
<td>Normal control (n=5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contralateral activation</td>
<td>3±0</td>
<td>3±0</td>
</tr>
<tr>
<td>Ipsilateral activation</td>
<td>0.4±0.5</td>
<td>1±0</td>
</tr>
<tr>
<td>Stroke patients (n=6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contralateral activation</td>
<td>2.7±0.5</td>
<td>2.5±0.8</td>
</tr>
<tr>
<td>Ipsilateral activation</td>
<td>0.2±0.4</td>
<td>2±0.6*</td>
</tr>
</tbody>
</table>

fMRI indicates functional MRI; NIRS, near-infrared spectroscopic topography; R Hand and L Hand, right- and left-hand movement.

Mean±SD. *P<0.05 vs control. Brain activation was scored 0 (no activation) through 3 (intense activation). All the stroke patients had left hemiparesis.
The findings of this study suggested that the stroke patients without severe residual hemiparesis after ischemic stroke of the MCA territory activated preexisting uncrossed motor pathways, which may have been accessed or recruited to compensate for damage to the crossed motor pathways by the stroke. In normal subjects, approximately 10% to 15% of the corticospinal tract has been thought to descend uncrossed.\textsuperscript{25} The relationship between the motor cortex and ipsilateral hand movements may be intensified after damage to the contralateral motor cortex. Furthermore, Shibasaki et al\textsuperscript{26} showed that the performance of the complex motor tasks was accompanied by a bilateral activation of motor cortices, although the performance of simple motor tasks resulted in only contralateral activation. Therefore, simple hand grasping requires only contralateral motor cortex in normal subjects, but paretic hand movements may need both motor cortices for execution of more effortful movements. Thus, compensatory changes may occur after stroke in the undamaged cortical tissue surrounding the infarct and in distant cortical tissue, including the unaffected hemisphere. The findings of this study strongly suggest an active role of the ipsilateral, unaffected hemisphere in the restoration of motor function, as has been reported by earlier studies using fMRI, PET, and transcranial magnetic stimulation.\textsuperscript{5–7}

All the 6 patients of this study had an infarct in the right hemisphere and exhibited left hemiparesis. This may be more than by chance because Kim et al\textsuperscript{27} reported that, although the right motor cortex was activated mostly during contralateral finger movements, the left motor cortex was activated substantially during ipsilateral finger movements in both right-handed and left-handed subjects. Therefore, left hemiparesis might recover better than right hemiparesis by recruiting more uncrossed motor fibers. But this hemispheric asymmetry in the functional activation during hand movements was not observed in our 5 control subjects. Another possibility is that a small number of subjects with relatively large hemispheric motor asymmetry (many ipsilateral fibers to the left hemisphere) may escape selectively from left hemiparesis after cerebral infarction in the right hemisphere. Because there is a report of a patient who exhibited ipsilateral hemiplegia after hemorrhagic stroke (in the right hemisphere),\textsuperscript{28} there might be considerable variability in the amount of uncrossed motor fibers among individuals. Further characterization of ipsilateral motor pathways remains to be explored. It is of interest to study patients with right hemiparesis or patients with more severe hemiparesis, but aphasia or difficulty in hand movement would make such studies complicated. Evaluation of patients at multiple time points after stroke needs to be performed to elucidate the mechanisms of the restorative process.

In conclusion, we demonstrated that both fMRI and NIRS allowed study of recovery of motor function after stroke. The findings of this study suggested that the recovery of hemiparesis after stroke was caused by motor cortical reorganization involving both the affected and unaffected hemispheres. fMRI has been an important tool in aiding our understanding of the mechanisms of poststroke motor recovery. In addition, we concluded that NIRS topography was useful for monitoring and studying poststroke brain function and for supplementing other imaging techniques because of its unique characteristics, such as compact portability, dynamic monitoring, and resistance to motion artifact.

References


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