

## Evidence of Cortical Reorganization in a Monoparetic Patient with Cerebral Palsy Detected by Combined Functional MRI and TMS

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—Abstract—

The motor recovery mechanism of a 21-year-old male monoparetic patient with cerebral palsy, who had complained of a mild weakness on his right hand since infancy, was examined using functional Magnetic Resonance Imaging (fMRI) and Transcranial Magnetic Stimulation (TMS). The patient showed mild motor impairment on the right hand. MRI located the main lesion on the left precentral knob of the brain. fMRI was performed on this patient as well as 8 control subjects using the Blood Oxygen Level Dependent technique at 1.5 T with a standard head coil. The motor activation task consisted of finger flexion-extension exercises at 1 Hz cycles. TMS was carried out using a round coil. The anterior portion of the coil was applied tangentially to the scalp at a 1.0 cm separation. Magnetic stimulation was carried out with the maximal output. The Motor Evoked Potentials (MEPs) from both Abductor Pollicis Brevis muscles (APB) were obtained simultaneously. fMRI revealed that the unaffected (right) primary sensori-motor cortex (SM1), which was centered on precentral knob, was activated by the hand movements of the control subjects as well as by the unaffected (left) hand movements of the patient. However, the affected(right) hand movements of the patient activated the medial portion of the injured precentral knob of the left SM1. The optimal scalp site for the affected (right) APB was located at 1 cm medial

to that of the unaffected (left) APB. When the optimal scalp site was stimulated, the MEP characteristics from the affected (right) APB showed a delayed latency, lower amplitude, and a distorted figure compared with that of the unaffected (left) APB. Therefore, the motor function of the affected (right) hand was shown to be reorganized in the medial portion of the injured precentral knob.

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**Key Words:** Functional magnetic resonance imaging, Motor recovery, Mapping, Magnetic stimulation

## INTRODUCTION

An understanding of the motor recovery mechanism is important for brain rehabilitation because it can provide the basis for scientific management. However, the precise nature of the motor recovery mechanism after a brain injury is unclear. Cramer et al.<sup>1, 2)</sup> reported that the post-stroke motor recovery mechanism consists of the following: reorganization of the injured motor cortex into the adjacent areas, unmasking of the ipsilateral motor pathway and activation of the supplementary motor area (SMA). Although many cases have reported reorganization of the ipsilateral motor pathways, there are few reports on the reorganization of the motor function into areas adjacent to the primary motor cortex (M1) lesion in humans.<sup>3-7)</sup> This study tried to demonstrate the motor recovery mechanism in a monoparetic cerebral palsy patient who showed mild motor weakness on the right hand and a major lesion on the left precentral knob, which is an area controlling the main motor function of the hand.<sup>8)</sup> This

case report suggests that the motor function of this patient underwent reorganization to the medial portion of the injured precentral knob of M1.

## CASE REPORT

A 21-year-old male, who had suffered mild weakness on the right hand since infancy, was referred to Yeungnam University Hospital for an evaluation. He was born at term without complications. His developmental milestones were mildly delayed. He could walk at the age of 2 years and showed a left hand dominancy from infancy. He had never undergone an examination in any hospital to determine the cause of the weakness in his right hand. At this evaluation, he showed very mild weakness on the right hand, and the grade of finger flexor/extensor on the right hand on manual muscle test was Good+. The fine motor ability of the right hand was mildly impaired to the extent that his purdue pegboard score was 8 (normal range: 14.6±1.9).<sup>9)</sup> The Fluid

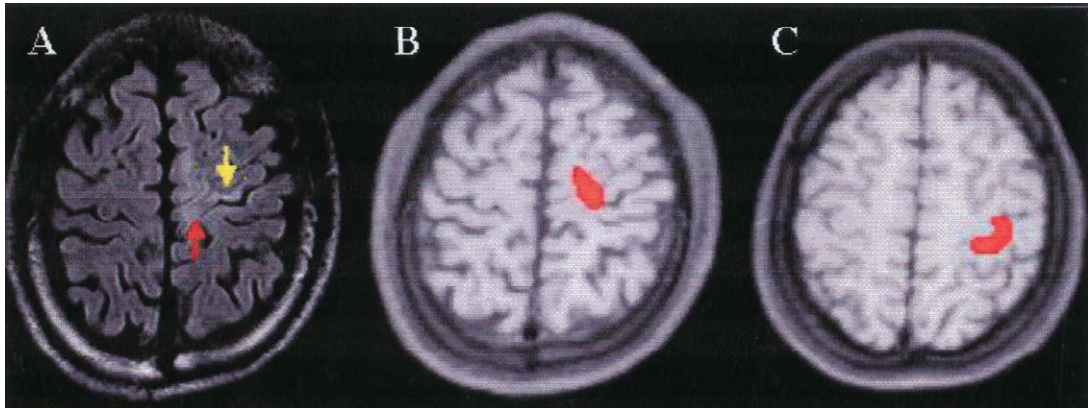


Fig. 1. Focal high signal intensity in the left precentral knob (yellow arrow), the medial portion of the left primary sensori-motor cortex (SMI) (red arrow), and the supplementary motor area, can be seen on the Fluid Attenuated Inversion Recovery (FLAIR) images of the brain MRI (A). Functional MRI shows activation of the medial portion of the injured precentral knob of the contralateral (left) SMI by the affected (right) hand movements (B), and the contralateral (left) SMI centered on the precentral knob was activated by the right hand movements of a control subject (C).

Attenuated Inversion Recovery (FLAIR) images of the brain revealed abnormal high signal intensity in the precentral knob (Fig. 1A, yellow arrow) in the medial portion of his left M1 (Fig. 1A, red arrow) as well as in his left SMA suggesting a perinatal injury (Fig. 1A). Eight healthy volunteers (4 women and 4 men; mean age 28 years, range 21 to 35 years) with no history of neurological disease were examined in order to compare the activated location of M1. All the subjects provided written informed consent prior to the study.

#### fMRI

The blood oxygenation level dependent (BOLD) fMRI measurement, which uses the Echo Planar Imaging (EPI) technique, was

performed on a 1.5 T MR scanner (Vision, Siemens, Erlangen, Germany) with a standard head coil. The T1-weighted images were obtained using a conventional spin-echo sequence for gross anatomical visualizations. For the motor task paradigm, the finger flexion-extension movements were performed at 1 Hz cycles for stimulation over a repeating cycle of 15 seconds rest and 15 seconds stimulus. The differences in the MR signal between the rest and stimulus periods were then analyzed using STIMULATE (CMR, U. of Minnesota), which is a software specializing in fMRI data analysis. Statistical maps indicating the activation patterns were generated using a Student's *t*-test. Pixels with a *p*-value <0.001 were determined to be activated. In addition, areas where 4 or

more pixels were activated simultaneously were selected for cluster analysis. Regions of interest were drawn around the primary sensori-motor cortex (SMI), premotor area (PMA) and SMA by a neuroradiologist. The fMRI image showed the activated area to be located medially to the injured left precentral knob, even though the contralateral (left) SMI was activated by the affected (right) hand movements (Fig. 1B). In contrast, the contralateral (right) SMI centered to the precentral knob was activated by the unaffected (left) hand movements of this patient as well as by the hand movements of all the control subjects (Fig. 1C).

## TMS

The Motor Evoked Potentials (MEPs) were obtained from both Abductor Pollicis Brevis muscles (APB) in the relaxed state. A cloth marked with spacings 1 cm apart and featuring Cz, the intersection of the midsagittal and inter-aural lines, was placed on the scalp as a reference and magnetically stimulated with a Dantec Mag2 stimulator and a 90 mm (mean diameter) round coil. Although a butterfly coil, which has a larger focus than large round coils, is ideal for locating the motor cortex, it is not strong enough to map the muscles with a higher threshold or small cortical representation areas.<sup>10)</sup> A round coil is stronger than a butterfly coil but it can induce widespread activation of many muscles and is not nearly

as focal.<sup>10)</sup> However, a round coil can also be used for motor cortex mapping through focal stimulation only if the anterior portion of the coil is placed tangentially close to the head and a low stimulation intensity is maintained.<sup>11)</sup> The round coil was used for mapping because the MEP was not evoked by the butterfly coil in this patient. Only the anterior portion of the coil was placed tangentially close to the scalp, while the handgrips were placed on sites parallel to the midsagittal line facing the back. The side marked A on the coil needs to be on the top when the left hemisphere is stimulated, and the reverse side should be on the top when the right hemisphere is stimulated. One site was stimulated 3 times at 1 cm intervals, from which the shortest latency and the average of the peak-to-peak amplitudes were adopted. The site showing the lowest ET, the shortest latency, and the largest average amplitude, was designated the optimal scalp site. Magnetic stimulation was undertaken at the maximal output. The optimal scalp site was found at (4, 0) of the unaffected (right) motor cortex for the unaffected (left) APB, and the ET was 45% (Fig. 2A). The optimal scalp site was present at (-3, 0) of the affected (left) motor cortex of the affected (right) APB, with the ET increasing to 85% (Fig. 2A). The latency of the contralateral MEP was prolonged to 26.5 msec (Fig. 2B). The amplitude of the contralateral MEP decreased to 570  $\mu V$ . The

## DISCUSSION

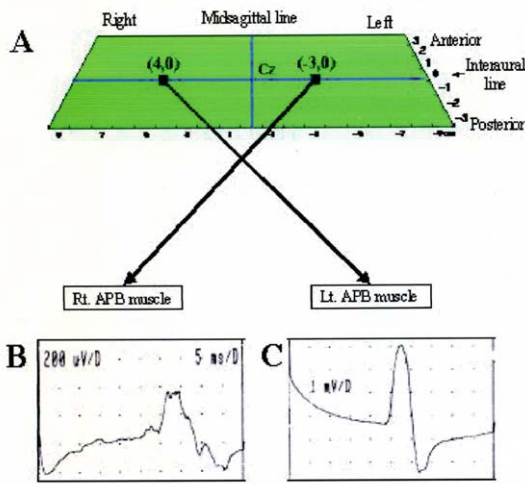


Fig. 2. Diagram of motor pathways evoked by transcranial magnetic stimulation, showing the optimal scalp site (-3, 0) of the affected (left) motor cortex, was located 1 cm medially, compared with the (4, 0) optimal scalp site of the unaffected (right) motor cortex (A). The Motor Evoked Potential (MEP) from the affected (right) APB (B) shows low amplitude, prolonged latency, and a distorted figure compared with that of the unaffected (left) MEP (C).

wave of the contralateral MEP was distorted (Fig. 2B). The contralateral MEPs to the right APB, from the left motor cortex, were evoked from 3 sites around the optimal scalp site. The latency and amplitude of the MEP, which was evoked at the left APB when stimulated at the optimal scalp site, was 23.5 msec and 5450  $\mu V$ , respectively (Fig. 2C). The contralateral MEPs to the left APB from the right motor cortex were evoked from 6 sites around the optimal scalp site.

Brain mapping is an indispensable tool for examining the recovery mechanism of an injured brain. Among the many non-invasive brain-mapping techniques, fMRI and TMS are utilized most frequently because they can be used repeatedly and produce no ionizing radiation. Furthermore, when employed in combination, they can provide the most accurate brain mapping of the motor function.<sup>12)</sup> fMRI, with its excellent spatial resolution, is particularly useful for confirming reorganization into the areas adjacent to an injured MI. On the other hand, TMS can provide information on the motor pathways through the characteristics of the MEP.<sup>13,14)</sup> This study used fMRI and TMS to evaluate the motor recovery mechanism of a paretic hand of a patient with the main lesion on the left precentral knob. The MEP characteristics of the unaffected (left) APB when stimulated at the optimal scalp site of the right motor cortex were normal.<sup>15,16)</sup> However, the MEP from the affected (right) APB showed a prolonged latency, low amplitude, increased ET, and a distorted figure when stimulated at the optimal scalp site of the affected (left) motor cortex. Considering the MEP characteristics from both motor cortices, it appears that cortical reorganization occurred after the precentral knob injury. In addition, fMRI revealed the medial portion of the injured precentral knob

of the affected (left) SMI to be activated by the affected (right) hand movements. This was never observed in the unaffected hand movements of this patient or in the hand movements of the control subjects. The optimal scalp site for the affected (right) APB was located 1 cm medially to that of the unaffected (left) APB. Overall, it appears that the motor function of the hand representation in the injured precentral knob had been reorganized into the medial portion of the injured precentral knob. The importance of perilesional reorganization was demonstrated in Rouiller's study which confirmed that reorganization into the areas adjacent to the injured M1. Moreover, among the three motor recovery mechanisms proposed by Cramer et al., this is the only recovery mechanism that is capable of maintaining the fine motor ability of the hand.<sup>1,17)</sup>

There have been several reports on the reorganization into the medial representation of an injured M1 in monkeys.<sup>18,19)</sup> The most famous study was reported by Nudo et al., who showed that the hand representation affected by the M1 injury, extended to the elbow and shoulder after they had been exercised to simulate rehabilitation in monkeys.<sup>19)</sup> There is no reference of hand representation in humans except for a slowly progressive disease e.g. a brain tumor.<sup>20)</sup> The reorganization of the adjacent intact cortex after a focal injury might represent the

recruitment of alternative sites for motor representation, which is possible because the corticospinal tract originates from many areas in the cerebral cortex.<sup>21-24)</sup> These areas include the premotor cortex, the parietal cortex and the mediolateral representation of M1. In humans, more than 50% of overlapping representations of the fingers have been reported to occur in M1.<sup>25)</sup> Therefore, it is believed that the reorganization involved in recruiting the corticospinal tract in this case originated from the medial representation of the precentral knob.

## 요 약

뇌성마비로 인해 오른 손에서 단부전마비를 호소하는 환자를 대상으로 기능적 자기공명영상 장치와 경두개 자기 자극기를 사용하여 운동신경의 회복기전을 연구하였다. 대상자는 21세 된 남자 환자로 오른손에 경미한 운동 기능의 손상을 보였고, 자기공명영상의 소견에서 좌반구의 precentral knob에서 병변을 보였다. 기능적 자기공명영상 촬영은 한 명의 대상자와 여덟 명의 정상인을 대상으로 표준화된 헤드 코일을 사용하여 1.5 T의 장치에서 BOLD 기술을 적용하여 실시하였다. 대상자들의 운동 수행은 1 Hz 주기로 손가락의 굴곡과 신전을 반복하는 과제가 제시되었다. 경두개 자기 자극은 원형 코일을 사용하여 코일의 앞쪽 부분이 대상자의 두피에서 1 cm 정도 떨어진 정점 부위에 적용되었고 양측의 짧은엄지별림근에서 발생한 운동 유발 전위가 동시에 측정되었다. 자기공명영상의 결과에서 환자의 비손상측(좌

측) 손과 정상군의 좌측 손의 운동 수행 시 오른쪽의 일차운동감각영역(SM1)의 precentral knob에서 활성도가 나타났다, 그러나, 환자의 손상측(우측) 손의 운동 수행 시, 좌측 일차운동감각영역의 손상된 precentral knob 내측 부위에서 활성도를 보였다. 또한, 경두개 자기 자극의 결과에서 손상측 짧은엄지벌림근에서 발생한 운동 유발 전위에 해당하는 뇌 부위가 환자의 정상측과 비교하여 1 cm 내측에서 발견되었다. 그러므로 손상측 손의 운동 기능이 손상된 precentral knob의 내측 부분으로 전위되어 신경재구성이 이루어진 것으로 추정되는 결론을 얻었다.

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