Effect of multiple subpial transection on motor cortical excitability in cortical dysgenesis

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Summary
We report here a 12-year-old patient with unilateral cortical dysgenesis and intractable simple partial seizure in his left arm, who underwent multiple subpial transection (MST) in the right cerebral cortex including the primary motor cortex. We investigated motor cortical excitability using multimodal transcranial magnetic stimulation (TMS) before and 1 month after MST, in which surgical cortical incisions were made with strokes 5 mm apart and 4 mm deep. Preoperative TMS studies showed hyperexcitability in the affected motor cortex as abnormally prolonged muscle responses to TMS with a wide cortical motor map, which were markedly reduced following the operation. The preoperative motor evoked potentials were large and polyphasic, and consisted of early and late components. The late component was completely abolished after MST, suggesting that this component might be due to activation of the corticospinal tract neurones by long recurrent axon branches of dysplastic excitatory pyramidal neurones, which were cut by MST, or by delayed, polysynaptic intracortical conduction with marked temporal dispersion. Intracortical inhibition in the affected motor cortex was also disrupted preoperatively and improved after MST. Postoperative recruitment order of muscle responses to TMS was bilaterally symmetrical, indicating that MST did not interfere with the function of the corticospinal tract neurones. The patient showed fair motor recovery and good seizure control after the operation. These results of TMS studies demonstrated the remarkable effectiveness of MST not only on intractable seizure but also on abnormal motor cortical organization and hyperexcitability in cortical dysgenesis.

Keywords: cortical dysgenesis; multiple subpial transection; transcranial magnetic stimulation; motor cortical excitability

Abbreviations: AT = active motor threshold; CSP = cortical silent period; ISI = inter-stimulus interval; MANOVA = multiple analysis of variance; MEP = motor evoked potential; MST = multiple subpial transection; RT = resting motor threshold; TMS = transcranial magnetic stimulation

Introduction
Multiple subpial transection (MST) was developed by Morrell and colleagues (Morrell and Hanbery, 1969; Morrell et al., 1989) and has been widely applied in a number of institutes as a novel surgical technique for treatment of intractable epilepsy in which the epileptogenicity originates in an eloquent cortex such as the sensorimotor cortex or language cortex (Shimizu et al., 1991; Devinsky et al., 1994; Sawhney et al., 1995; Wyler et al., 1995; Morrell et al., 1999). The aim of MST is to impair the capacity of cortical tissue to generate sufficient neuronal synchrony to produce epileptiform discharges, without interfering with its capacity to mediate normal physiological functions (Morrell et al., 1999). MST usually induces no or minimal postoperative functional alterations, which is attributable to preservation of cortical vertical columns, the master organization principle of the cortex (Morrell et al., 1999). Detailed reports on sensorimotor physiological changes after MST, however, have been limited. To our knowledge, there has only been one abstract, by Hoeppner and colleagues (Hoeppner et al., 1991), describing acute loss of somatosensory evoked potentials to nerve stimulation after MST, although the detailed mechanism remains unknown. With regard to motor functions following MST of the motor cortex, we cannot obtain any physiological insight by reviewing the literature.

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except for actual postoperative fair motor recovery (Morrell et al., 1999). After MST, patients’ motor function recovers up to the preoperative level following a transient phase of hemiparesis. Only a loss of finger dexterity sometimes remains, but it does not usually interfere with the patients’ daily life.

Cortical dysgenesis has been shown to be a more frequent aetiopathological mechanism of epilepsy by recent MRI studies than previously considered (Barkovich, 1995; Raymond et al., 1995). This rare syndrome is characterized as involving malformation of cortical development or neuronal migration disorder (Raymond et al., 1995; Sisodiya, 2000), and is characterized by a lack of normal cortical lamination or a disorganized cortical neuronal network. Motor developments in cortical dysgenesis are variable among patients but are often severely disturbed (Palmieri et al., 1991). There have been few reports of physiological motor function in patients with cortical dysgenesis using transcranial magnetic stimulation (TMS) (Maegaki et al., 1995). TMS is widely used as a non-invasive, painless technique to investigate motor cortical organization and excitability because it activates the corticospinal tract neurons trans-synaptically (Rothwell et al., 1991; Rossini and Rossi, 1998; Hallett, 2000). Assessment of motor cortical excitability is possible by diversified TMS variables such as threshold to stimulation (Rossini et al., 1994), cortical motor mapping (Wassermann et al., 1992), cortical silent period (Inghilleri et al., 1993) and intracortical inhibition or facilitation measured by a paired-pulse paradigm (Kujirai et al., 1993; Pascual-Leone et al., 1998).

In the present study, we investigated a patient with unilateral cortical dysgenesis who underwent MST of the motor cortex for intractable epilepsy using multimodal TMS techniques. The aim of this study was to investigate changes in the motor cortical organization and excitability after making surgical incisions in the primary motor cortex and surrounding cortical areas, and to discuss the pathomechanism on the motor function in cortical dysgenesis. The patient showed preoperative hyperexcitability limited to the affected motor cortex expressed as abnormally prolonged or delayed muscle responses to TMS, a wider than normal cortical motor map and disruption of the usual pattern of intracortical inhibition, all of which were markedly improved after MST accompanied by fair recovery of motor function and good seizure control.

Case report
A 12-year-old boy was admitted to our hospital with intractable simple partial seizures in May 1998. His seizures started at age 2 years, and consisted of simple partial seizures marching from the left arm to the eyelids, left hemiclonus and falling attacks. Since age 6 years, the seizures had become intractable despite use of antiepileptic drugs. Motor and mental development was normal. On admission, the simple partial seizures in his left arm occurred every day. He had no weakness or spasticity, and he could move the bilateral individual fingers in a complex fashion. Deep tendon reflexes were normal, and there was no Babinski’s sign. Mild mirrored movement was observed in the right hand when he attempted to move the left hand or fingers. He had no sensory dysfunction. His intellectual performance was within the normal range (IQ = 91). Scalp EEG showed spikes and sharp waves predominantly in the right frontocentral and parietal regions. Brain MRI showed blurring of the grey–white matter junction and abnormally high intensity signals in the right frontal region on T2-weighted images (Fig. 1). Thick cortical ribbons were also observed. The lesions were limited to the right hemisphere, and distributed over the precentral gyrus, superior frontal gyrus and paracentral lobule. The postcentral gyrus, middle frontal gyrus, temporal lobe and hippocampus appeared intact on MRI. There was also heterotopic grey matter adjacent to the right lateral ventricle. Results of brain single-photon emission computed tomography were unremarkable. Somatosensory evoked potentials to median nerve electrical stimulation showed symmetrical N20s, with no ‘giant’ cortical responses and no responses ipsilateral to the stimulated side. His preoperative antiepileptic medication included carbamazepine 400 mg and clonazepam 1.25 mg per day.

In June 1998, MST was performed on the right cerebral hemisphere under general anaesthesia, in accordance with the description by Morrell and colleagues (Morrell et al., 1989) as shown schematically in Fig. 2A. After craniotomy and exposure of the right cerebral cortex, the primary sensory and motor cortices were identified by somatosensory evoked potentials to left median nerve electrical stimulation. Then, the electrocorticogram was recorded, and the cerebral cortex showing epileptiform discharges was transected subpially with strokes 5 mm apart and 4 mm deep using a curved transector. The direction of the transection was perpendicular to the long axis of the gyrus. The cortical areas where MST was actually performed in the patient are shown in Fig. 2B, and included the right primary sensorimotor area over the central sulcus, the right superior and middle frontal gyri and the paracentral lobule (parts of areas 6 and 8). The Broca’s speech area was spared. The transected cortical areas were larger than the abnormal areas on the preoperative MRI. Cortical oozing was minimal, and there were no obvious intraoperative complications such as venous bleeding. A small biopsy specimen was obtained from the superior frontal gyrus during the operation (Fig. 2B). After the operation, the patient transiently exhibited left hemiparesis, but recovered in a week up to the preoperative level. Neurological examination 1 month after the operation showed no weakness, no spasticity and no obvious sensory disturbance, with deep tendon reflexes being within the normal range. He showed mild loss of finger dexterity in the left hand. His gait was normal. Neuropathological investigation of the biopsy specimen showed a variety of dysplastic cellular elements including disorganized cortical neurones without polarity and immature oligodendroglial cells with the appearance of
Fig. 1 Brain MRIs of the patient before (A) and 1 month after (B) multiple subpial transection (MST). Left images represent axial T₂-weighted images, and right images represent axial fluid attenuated inversion recovery images. Arrows indicate the central sulcus. Arrowheads in A indicate thick cortical ribbons and blurring of the grey–white matter junction. The postoperative MRIs showed that the brain damage was slight after MST, with no significant CSF shift around the operated cortex. Arrowheads in B indicate high intensity signals made by the surgical incisions in the precentral gyrus. L and R indicate left and right, respectively.

perivascular glial satellitosis, being mixed with neurones of normal appearance, which confirmed the diagnosis of cortical dysgenesis as previously reported in an abstract form (Komori et al., 1999). Brain MRI 1 month after the operation showed no obvious brain damage or significant CSF shift around the operated hemisphere (Fig. 1B). Over a 2-year follow-up since the operation, the frequency of the seizures has decreased markedly to about once every 6 months with constant...
Multiple subpial transection and cortical excitability

Fig. 2 (A) Schematic figure of multiple subpial transection (MST) (modified from the figure in Morrell et al., 1989). (B) Schematic cortical areas where the MST was performed in the patient, as shown by the incision line of the cortical surface. The cortex itself is not the patient’s own cortex. The small black circle on the superior frontal gyrus indicates the biopsied cortical region.

administration of the same antiepileptic drugs as given preoperatively. He is now attending school and enjoying playing tennis with his friends.

Methods
We performed the following TMS studies before and 1 month after MST. We obtained the written informed consent of the patient and his parents, and the study was approved by the Tokyo Metropolitan Neurological Hospital Ethics Committee.

The patient was seated on a comfortable reclining chair. For focal TMS, we used a figure-of-eight coil (mean diameter 70 mm) connected to a Magstim 200 stimulator (Magstim Company, Whitland, Dyfed, UK). Motor evoked potentials (MEPs) were recorded via surface electrodes attached in a belly tendon montage from the flexor carpi radialis muscle. We first tried to examine the first dorsal interosseous muscles, but the preoperative resting motor threshold determined by the criteria described below was 66% for the left first dorsal interosseous and 90% for the right first dorsal interosseous. This threshold for the right first dorsal interosseous was too high for the subsequent examinations, and therefore we focused on only the flexor carpi radialis muscles. The coil was placed tangentially to the scalp, with the handle pointing backwards. The direction of electric current in the coil junction was from anterior to posterior. Responses were amplified and filtered through a Counterpoint electromyograph (Dantec Co. Ltd, Denmark), with the band-pass ranging from 10 to 5 kHz, a sweep time of 500 ms and a sampling rate of 10 kHz. Data were inspected on-line and stored on the hard drive of an IBM-compatible computer for off-line analysis.

TMS threshold
We defined the excitability thresholds in relaxed and tonically active muscles [the resting motor threshold (RT) and the active motor threshold (AT), respectively]. RT was the stimulator output (%) required to produce an MEP of 100 µV in amplitude in at least three of six successive trials during complete muscle relaxation monitored by auditory and visual feedback (Rossini et al., 1994). AT was the minimum stimulus intensity (%) that evoked a clearly distinguishable MEP from the background EMG activity in at least three of six consecutive stimuli during flexor carpi radialis contraction that induced wrist flexion from a horizontal level with as slight a contraction force as possible (<10% of maximal contraction force). The site of magnetic stimulation on each hemisphere was the ‘hot spot’ for the contralateral flexor carpi radialis where the largest MEPs with the shortest latencies were obtained.

TMS mapping
TMS mapping on each hemisphere was carried out for the contralateral flexor carpi radialis muscle (Wassermann et al., 1992). First, the ‘hot spot’ for the flexor carpi radialis was searched by moving the coil on the scalp, and the RT was determined at the ‘hot spot.’ Stimulus intensity was set at 120% RT for each flexor carpi radialis under complete
relaxation of the muscle. Scalp stimulation sites were determined using a snugly fitting plastic cap, pre-marked with sites at 1 cm intervals in a latitude–longitude coordinate system. The first site stimulated was over the estimated centre of the hand motor area (‘hot spot’), and the area was then mapped until the border had been defined. TMS maps were generated after calculating the averages of area (mV × ms) under the MEP curve from the onset to returning to baseline (MEP area) of four consecutive MEPs for each stimulation site. In the maps, the vertex was represented as $x = 0$ and $y = 0$, where the $x$-axis was the interaural line and the $y$-axis was the nasion–inion line. The anterior and rightward directions were defined as positive.

**Intracortical inhibition**

We investigated intracortical inhibitory function within the motor cortex using a paired TMS technique (Kujirai et al., 1993). We used two Magstim 200 stimulators connected to a Bistim device (Magstim Company, Whitland, Dyfed, UK). MEPs were recorded from the completely relaxed flexor carpi radialis muscles contralateral to the stimulation. The conditioning stimulus intensity was 5% below the AT, and the test stimulus intensity was set at 130% RT. In measuring the AT and RT, the second magnetic stimulator remained switched on in standby mode. Inter-stimulus intervals (ISIs) were varied from 1 to 10 ms. Non-conditioned (control) and conditioned test stimuli were intermixed randomly. We collected eight control and conditioned responses for each ISI, and measured MEP areas. Thereafter, the mean MEP area of the conditioned response was expressed as a percentage of that of the control response (MEP area ratio). The results were also compared with the data of 10 healthy control subjects including the authors (four women and six men; mean age 32.3 years). For statistical analysis of changes in MEP size at each ISI, we used multiple analysis of variance (MANOVA) for the control subjects, and Mann–Whitney $U$ test for the patient. The level of significance was set at five per cent.

**MEP recruitment and cortical silent period**

To evaluate recruitment order of corticospinal tract and cortical silent period (CSP), we stimulated each motor cortex with stimuli of increasing intensity (Inghilleri et al., 1993; Cicinelli et al., 2000). This examination was performed after the operation to check the effects of MST on MEP recruitment of the operated motor cortex and to compare it with that of the non-operated motor cortex. In addition, we roughly compared the postoperative results with preoperative incomplete data. In the postoperative study, the stimulus intensity was increased from the AT up to 240% AT, in steps of 20% of the AT, using a single Magstim 200 stimulator. In the preoperative incomplete study, the stimulus intensity was set at 40, 50, 60 and 70% of the stimulator output. The patient was requested to flex the wrist with a slight contraction force as described above for measuring the AT. MEPs were recorded from each flexor carpi radialis muscle after TMS on the contralateral motor cortex. In the postoperative study, we collected eight consecutive responses for each stimulus intensity level, and calculated the average MEP area and CSP duration. Preoperatively, we collected a few responses at each intensity. The CSP was measured as the interval between the time of magnetic stimulation and visible resumption of EMG activity following the CSP, with a gain of 0.2 mV/cm. We compared the results of MEP area and CSP between the bilateral flexor carpi radialis muscles, using MANOVA (with $P < 0.05$ considered statistically significant).

**Ipsilateral MEP**

We studied whether TMS produces MEPs from the active flexor carpi radialis ipsilateral to the site of stimulation. For this examination, the patient was requested to contract the flexor carpi radialis muscles with maximal contraction force. Stimulus intensity was set at 100% of the output. An averaging technique was not used.

**Results**

**TMS threshold**

The RTs and ATs in the preoperative study were 60 and 38% for the left flexor carpi radialis, and 64 and 40% for the right flexor carpi radialis, respectively. Those in the postoperative study were 64 and 40% for the left flexor carpi radialis, and 62 and 38% for the right flexor carpi radialis, respectively. The threshold variation between the pre- and postoperative studies was within 5%.

**TMS mapping**

In the preoperative study, TMS on the unaffected (left) hemisphere evoked monophasic MEPs with normal appearance and relatively small amplitudes (Fig. 3A). In contrast, TMS on the affected (right) hemisphere evoked abnormally polyphasic MEPs with larger amplitudes and longer durations than those on the opposite side (Figs 3A and 4). In general, the polyphasic MEPs consisted of early and late components, and in the periphery of the cortical map some responses had dominantly or only the late components with onset latencies of 30–35 ms (Fig. 3A and the lower two traces in Fig. 4). The latencies of the early components were 15–17 ms, similar to those in the opposite flexor carpi radialis. The map area on the right hemisphere was larger (37 excitable sites) than that on the left hemisphere (19 excitable sites). In the postoperative study, the MEP waveforms and map area on the left hemisphere were almost the same as those determined preoperatively (23 excitable sites). For the right hemisphere, the MEP waveforms showed a marked change, becoming monophasic with short latencies and small amplitudes, probably consisting of only the early
components in the preoperative study (Fig. 3B and the upper two traces in Fig. 4). The delayed components were entirely abolished. The map area of the right hemisphere was also reduced after the operation (20 excitable sites).

**Intracortical inhibition**

In healthy control subjects, significant inhibition was noted at ISIs of 1–5 ms ($P < 0.0001$, MANOVA) as previously reported (Kujirai et al., 1993) (Fig. 5C and D). In the preoperative study for the patient, the right flexor carpi radialis showed similar inhibition at ISIs of 1–3 ms ($P < 0.05$, Mann–Whitney U test), but the left flexor carpi radialis did not show inhibition at any ISI (Fig. 5A and C). At ISI 1 ms, the conditioned MEPs in the left flexor carpi radialis showed disappearance of the late components although the inhibition was not significant due to variability of responses. In the postoperative study, the right flexor carpi radialis showed results similar to those obtained preoperatively (Fig. 5B and D). The left flexor carpi radialis also showed significant inhibition at ISIs of 1–3 ms, which was not observed in the preoperative study ($P < 0.05$, Mann–Whitney U test).

**MEP recruitment and CSP**

In the preoperative study, areas of MEPs during voluntary contraction progressively increased with increasing stimulus intensity (Fig. 6). At stimulation with 70% output, the MEP areas and CSPs were 72.3 mV × ms and 108 ms for the left flexor carpi radialis on average, and 42.0 mV × ms and 92 ms for the right flexor carpi radialis, respectively. The late component seen in the MEPs during resting in the TMS mapping study was hidden in the MEPs with short latencies during contraction. Statistical analysis was impossible due to the small sample numbers. In the postoperative study, the MEP areas for each flexor carpi radialis also progressively increased with increasing stimulus intensity, and there were no significant differences in the recruitment orders between the bilateral flexor carpi radialis muscles (MANOVA) (Fig. 7A and B). On the other hand, the CSPs in the left flexor carpi radialis showed no prolongation with increasing stimulus intensity, while those in the right flexor carpi radialis showed some incomplete prolongation effect (Fig. 7A and C). The CSP progression curves were significantly different between the bilateral flexor carpi radialis muscles ($P < 0.0005$, MANOVA).

Fig. 3a.
Ipsilateral MEP
No ipsilateral MEPs were elicited in the bilateral flexor carpi radialis muscles in the pre- or postoperative studies.

Discussion
The present study in a case of unilateral cortical dysgenesis clearly showed the effectiveness of MST not only on the seizures but also on the abnormal excitation/inhibition properties and output of the affected motor cortex. Judging from the postoperative MRI findings, the effect of craniotomy or CSF shift after the operation on the TMS results could be ruled out.

The brain MRIs of the patient and the pathological findings of the biopsy specimen indicated that he had unilateral cortical dysgenesis or neuronal migration disorder (Yagishita et al., 1997; Chan et al., 1998; Komori et al., 1999). Since the advent of MRI, cortical dysgenesis has been shown to be one of the most important causes of intractable epilepsy (Raymond et al., 1995). MRI studies have shown that areas of focally thick cortices, broad gyri, blurring of the grey–white matter junction and T2-weighted abnormal signals of the white matter are more frequent than previously suspected and are responsible for many epileptic disorders previously considered cryptogenic (Yagishita et al., 1997). Microscopically, cortical dysplastic lesions are characterized by a lack of normal cortical lamination, which may be associated with abnormal giant neurones, and occasionally also with bizarre large eosinophilic, so-called balloon cells (Taylor et al., 1971; Ferrer et al., 1992; Sprefico et al., 1998). Dendrites and axons are often oriented and distributed abnormally (Desbiens et al., 1993).

Cortical dysplastic lesions are highly and intrinsically epileptogenic (Mattia et al., 1995; Palmini et al., 1995), and excision of epileptogenic cortical tissue or functional surgery such as MST is often crucial for seizure control. In the abnormal multilaminar cortical organization in neuronal migration disorders, dysfunctions at the level of the cortical synaptic circuits lead to abnormal neuronal synchronization, which will induce epileptogenicity. Previous immuno-

![Diagram](image)

Fig. 3 Motor evoked potentials (MEPs) recorded from each flexor carpi radialis muscle after TMS of the contralateral hemisphere before (A) and 1 month after MST (B). Two recordings were superimposed for each stimulation site, which were 1 cm apart over each hemisphere. Cz represents the vertex. L and R indicate the left and right hemisphere, respectively. The horizontal and vertical scale bars represent 50 ms and 2 mV, respectively. The map graphs beneath the MEP waveforms were made from the MEP area values at each stimulation site. One grid on the horizontal plane in the map graphs represents 1 cm.
The MEP recruitments in the active muscles were symmetrical vertical columnar organization and the plastic capability of the motor cortex periphery produced MEPs predominantly with a cellular function within the cortex (Jones et al., 1990). That the corticospinal tract itself in the operated cortex could activate the motor cortex. The presence of the map periphery predominantly showing the late component suggests that the delayed activation was not by current spread but via relatively long recurrent axonal conduction of the corticospinal tract neurones. The postoperative map, which showed disappearance of the late component after the cortical transection with strokes 5 mm apart, also supported this idea. These axon branches were probably longer than the axons of the inhibitory interneurones because the intracortical inhibition in the paired-pulse paradigm was improved after MST.

The unique surgical technique MST is based on the following experimental background: (i) the functional integrity of the cortex is dependent to a large degree on its vertical columnar organization (Mountcastle, 1957; Asanuma and Sakata, 1967); (ii) vertically oriented surgical slicing failed to impair cortical behaviour (Sperry et al., 1955); and (iii) studies of experimental epileptogenesis established the mode of propagation of epileptic activity along horizontal fibres and determined the minimal volume of transversely arranged contiguous cortical tissue necessary for its generation (Morrell, 1969; Tharp, 1971). Within the cortex, Golgi type II cells, basket cells, and most other interneurones relay information in a vertical cascade terminating on the apical dendrites of the pyramidal cells. Within the vertical column, the thalamocortical afferent input to all its layers, and the primary efferent outflow from layers III and V, have vertical axon trajectories (Asanuma, 1975), which remain uncut in MST. On the other hand, the horizontal fibre network has an important role in local recurrent inhibitory and excitatory interactions underlying flexibility and plasticity of cellular function within the cortex (Jones et al., 1978). MST is based fundamentally on the crucial functional role of the vertical columnar organization and the plastic capability of the horizontal fibre network.

Neural activity in the cerebral neocortex is highly synchronous during epileptic seizures, and this synchronous excitatory interactions underlying flexibility and plasticity of cellular function within the cortex (Jones et al., 1978). MST is based fundamentally on the crucial functional role of the vertical columnar organization and the plastic capability of the horizontal fibre network.
Fig. 5 Effects of subthreshold conditioning magnetic stimulation on control (non-conditioned) MEPs at varied inter-stimulus intervals (ISIs), before (A and C) and after (B and D) MST. (A and B) Representative control and conditioned MEP waveforms. Two recordings were superimposed for each ISI. Left and right indicate the left and right flexor carpi radialis muscle, respectively. The horizontal and vertical scale bars represent 50 ms and 0.5 mV, respectively. (C and D) The curves as percentages of the mean conditioned MEP area to the control MEP area for the right (circles) and left (squares) flexor carpi radialis muscles of the patient before (C) and after (D) MST. Triangles indicate mean values of 10 healthy control subjects. Vertical bars represent standard deviations. Values below 100% indicate inhibition. Closed symbols indicate statistically significant inhibition ($P < 0.05$, using MANOVA for the control subjects and Mann–Whitney $U$ test for the patient). Control MEP area is represented by horizontal dashed lines.
activity is initiated and coordinated by intrinsic cortical circuits (Mattia et al., 1995). In general terms, cortical neurones consist of pyramidal excitatory neurones and non-pyramidal inhibitory neurones. Previous experimental studies showed that when intracortical inhibition to non-pyramidal neurones was suppressed, all neocortical neurones displayed prolonged depolarizing events, arising largely from excitatory synaptic currents by pyramidal excitatory neurones, which might lead to epileptiform activity (Hablitz, 1988; Chagnac-Amitai and Connors, 1989). In particular, intrinsically bursting pyramidal neurones in middle cortical layers play a central role in initiating widespread synchronous activity within the cortex under conditions in which synaptic inhibition is abolished. Horizontal fibres within the cortex, which might be cut by MST, are composed mainly of recurrent axon branches and basal dendrites of pyramidal excitatory neurones, and axons of stellate or basket inhibitory interneurones. MST in our patient might have improved abnormal synchronization in excitatory pyramidal neurones by cutting their recurrent axon branches and basal dendrites rather than axons of inhibitory interneurones.

There have been a number of reports of increased motor cortical excitability studied by TMS in patients with various types of epilepsy: focal or generalized; partial or complex seizures; and cortical myoclonus epilepsy (Reutens and Berkovic, 1992; Reutens et al., 1993; Brown et al., 1996; Caramia et al., 1996; Brodmann et al., 1999; Cicinelli et al., 2000). Although antiepileptic drugs are known to modify the cortical excitability (Ziemann et al., 1996), such an effect after MST in our patient was unlikely since we did not change the antiepileptic drugs after the operation. TMS studies concerning cortical dysgenesis have been limited, and this is, to our knowledge, the first report of abnormal motor cortical output and excitatory/inhibitory properties in addition to the effectiveness of MST in cortical dysgenesis. The postoperative findings in our patient confirmed not only the effectiveness of MST on seizures but also the objective evidence that MST does not interfere with the corticospinal tract function (Leonhardt et al., 2000). Although we have no TMS data after long-term follow-up in our patient, we believe that the long-lasting effectiveness of MST on seizures suggests the continuously effective disconnection of the intracortical abnormal synchronous neuronal networks.

In general, the actual dysplastic areas in cortical dysgenesis are often larger than the abnormal areas on MRI. Also, in our patient, the postcentral and middle frontal gyri, which did not show MRI abnormality preoperatively, showed epileptiform discharges during the operation, and MST entirely covered the cortical areas showing the abnormalities on MRI. Although precise comparison between the motor map size and the distribution of the dysplastic areas is rather difficult, the wide TMS map extending to the anterior, lateral and posterior directions indicates that the abnormally excitable cortical areas in the motor map were larger than the abnormal areas on MRI, which was consistent with the wider distribution of the intraoperative epileptiform discharges. The long-lasting effectiveness of MST in our patient indicates that the MST area was sufficiently wide and, therefore, that the dysplastic lesions were not widespread over cortices supposed to be intact at the time of operation. Extended MST is often necessary in patients with intractable epilepsy (Shimizu et al., 1991), and preoperative TMS mapping might predict the extent of MST.

In healthy subjects, CSP usually shows progressive prolongation with increasing stimulus intensity independently of MEP size (Inghilleri et al., 1993; Cicinelli et al., 2000). In the postoperative study, the affected motor cortex showed no CSP prolongation with increasing stimulus intensity, while the intact motor cortex showed incomplete but significantly different prolongation. Since we did not investigate the MEP recruitment and CSP before MST in a rigorous manner, it remains unknown whether the postoperative CSP asymmetry could be ascribable to the effect of MST or to cortical dysgenesis itself. However, the preoperative CSP length (108 ms) for the left flexor carpi radialis at stimulation of 70% output was longer than that determined postoperatively (82 ± 6 ms) at stimulation of 180% AT (= 72% output) (Figs 6 and 7), suggesting the effect of MST. CSP is influenced from various cortical and even subcortical regions, suggesting multilevel and polysynaptic origins of CSP (Classen et al., 1997; Shimizu et al., 1999). The shorter CSP in the operated cortex might indicate that MST interfered with polysynaptic inhibitory modulation within the motor cortex. The neuronal population responsible for CSP, which is activated with strong TMS, is different from neurones for intracortical inhibition in a paired-pulse study with weak TMS, and the postoperative shorter CSP is not contradictory to the improved intracortical inhibition in the paired-pulse study.

We used several parameters to evaluate the motor cortical excitability: resting and active motor thresholds; TMS maps; intracortical inhibition or facilitation by a paired-pulse paradigm; and MEP recruitment order (Pascual-Leone et al., 1998). In our patient, the thresholds showed no remarkable
Fig. 7 Postoperative MEP recruitments with increasing stimulus intensity. (A) MEP waveforms at each stimulus intensity that was described in the leftmost column as percentages of the active motor threshold (AT). The actual intensities as percentages of the stimulator output are shown beneath the MEP traces. Asterisks indicate the end-points of the CSPs for individual MEPs. Left and right indicate the left and right flexor carpi radialis muscle, respectively. The horizontal and vertical scale bars represent 50 ms and 2 mV, respectively. (B and C) Stimulus–response curves of MEP areas (B) and CSPs (C) for the right (open circles) and left (open squares) flexor carpi radialis muscles during voluntary contraction. MEP areas and CSPs at each stimulus intensity are represented as the means and standard deviations (vertical bars). Stimulus intensities are presented as percentages of the active motor threshold. There was a significant difference in the CSP between the bilateral flexor carpi radialis muscles (*P < 0.0005, MANOVA).
changes after the operation, but significant changes were observed in the TMS maps and intracortical inhibition. Jennum and Winkel mentioned in their review article on TMS in epilepsy that it is uncertain whether mapping of the motor cortex is useful in presurgical evaluation of patients with intractable epilepsy (Jennum and Winkel, 1994). The present study, although only a single case study, indicated the value of TMS mapping to assess changes in motor cortical excitability after surgery. A single-pulse TMS is now considered to be safe even in epilepsy, as it seldom induces critical seizures (Tassinari et al., 1990; Jennum and Winkel, 1994; Ziemann et al., 1998; Cantello et al., 2000). Surgical intervention in the cerebral cortex may markedly change its physiological function, which requires precise physiological evaluation before and after surgery (Shimizu et al., 2000). TMS should be utilized in epilepsy research to evaluate how the motor cortex will function after surgery.

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