Changes in Distributed Motor Network Connectivity Correlates With Functional Outcome After Surgical Resection of Brain Tumors

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BACKGROUND: In patients with brain tumors around the motor cortices, deterioration of motor performance may be observed even if the integrity of the cortical output is maintained. Especially, resection of medial premotor area (PM) can cause postoperative deterioration called supplementary motor area syndrome.

OBJECTIVE: To clarify the neuronal mechanisms underlying postsurgical deterioration with a case-control study.

METHODS: Twelve patients with brain tumors underwent preoperative and postoperative sessions consisting of motor performance evaluation and 3T-magnetic resonance imaging data acquisition. Based on additional postsurgical motor deficits, 6 patients were classified into "deficit group," and 6 others were into "no deficit group." Using resting-state functional magnetic resonance imaging (fMRI), the integrity of functional connectivity was evaluated by placing a seed in the ipsilesional primary motor area (M1). With motor task fMRI, hand and foot representations were identified in the M1 and lateral and medial PMs. Probabilistic tractography assessed anatomic connectivity in the cortico-cortical and corticofugal networks.

RESULTS: Functional connectivity among M1 and lateral and medial PMs during resting-state fMRI was reduced postoperatively in the deficit group ($P < .05$, corrected) and preserved in the no deficit group. The deficit was unlikely to be attributable to surgical resection of specific anatomic connectivity. The amplitude of motor-evoked potential was maintained in available cases. These intraoperative observations agree with imaging findings suggesting preserved anatomic connectivity of the estimated corticofugal pathway.

CONCLUSION: The present findings suggest that supplementary motor area syndrome is caused by disorganization of functional connectivity among cortical motor networks rather than resection of anatomic connectivity of corticofugal pathway.

KEY WORDS: Large scale network, Premotor area, Primary motor area, Resting-state functional MRI, Tractography, SMA syndrome

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ABBREVIATIONS: BOLD, blood oxygen level–dependent; **fMRI,** functional magnetic resonance imaging; **FSL,** FMRIB software library; **M1,** primary motor area; **MEP,** motor evoked potential; **MNI,** Montreal Neurological Institute; **PM,** premotor area; **SMA,** supplementary motor area.

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In patients with brain tumors around the motor cortices, preservation of motor function remains a challenge. Motor-evoked potential (MEP) monitoring is one of the standard measures during brain surgery because MEPs are believed to indicate the integrity of the motor cortical output.[1,2] However, deterioration of motor performance may be observed even without disappearance of intraoperative MEPs. Especially, tumor removal in the medial premotor area (PM) can cause postoperative deterioration called supplementary motor area (SMA) syndrome.[3-5]

The spontaneous blood oxygen level–dependent (BOLD) fluctuations measured with resting-state functional magnetic resonance imaging (fMRI) are not random noise, but rather fluctuations in neuronal activity that are correlated within distinct functional networks.[6] Without task performance, strong coherence is reproducibly present among functional networks.[7,8] By contrast, tractography based on diffusion-weighted imaging (DWI) can visualize the in vivo dissection of white matter bundles. This noninvasive technique is now widely applied for preoperative evaluation in neurosurgery to trace major anatomic white matter fibers related to brain functions.[9,10]

This study aimed to clarify the neuronal mechanisms underlying postsurgical deterioration of motor performance in patients with SMA syndrome. Our first hypothesis was that the deterioration would occur as a result of insult to a specific motor cortex or the cortico-cortical fiber tract. Our second hypothesis was that the deterioration would reflect the deficits in a set of motor cortical areas or their fiber tract connections organizing functional and/or anatomic networks. The third hypothesis was that the deterioration would result from injury to the corticofugal fiber bundles of motor cortices, especially from nonprimary motor areas, which may be difficult to be monitored by MEPs. In this study, we examined these hypotheses by assessing resected areas with structural magnetic resonance imaging (MRI), functional connectivity with resting-state fMRI, and anatomic connectivity with tractography.

METHODS

Subjects

We recruited 12 consecutive patients (7 male patients; Table 1) who underwent resection of a brain tumor within or adjacent to motor

TABLE 1. Summary of Patient Details

Group	Case	Age/sex	Tumor location	Lesion side	Preoperative symptom	Tumor pathology	MEP monitoring/awake craniotomy	Fugl-Meyer assessment				Motor function outcome at 3 mo after surgery
								Hand (total 66)		Foot (total 34)		
								Pre	Post	Pre	Post	
Deficit	1	41/M	IFG, PrCG, PoCG, PCL	Left	Seizure	Oligodendroglioma	Y/Y	66	65	34	27	Mild motor weakness
	2	55/F	PrCG, IFG	Left	Seizure, hemiparesis	Glioblastoma	N/N	64	41	23	5	Mild motor weakness
	3	28/M	PCL, PCu	Right	Seizure	DNT	Y/Y	66	65	34	31	Full recovery
	4	34/F	SFG	Right	Seizure	Diffuse astrocytoma	Y/Y	66	63	34	27	Full recovery
	5	36/F	SFG, MFG	Left	Seizure	Anaplastic astrocytoma	Y/Y	66	41	34	20	Full recovery
	6	29/M	SFG	Left	Seizure	Diffuse astrocytoma	Y/Y	66	56	34	27	Mild motor weakness
No deficit	7	19/F	AG, SMG, PoCG	Left	Seizure	DNT	N/Y	66	66	34	34	—
	8	44/F	AG, SMG, PoCG	Left	Seizure	Diffuse astrocytoma	N/Y	66	66	34	34	—
	9	73/M	SFG	Right	Seizure	Glioblastoma	Y/N	66	66	34	34	—
	10	44/M	SFG	Right	Seizure	Oligodendroglioma	Y/Y	66	66	34	34	—
	11	16/M	MFG, IFG	Left	Seizure	Glioblastoma	Y/Y	66	66	34	34	—
	12	26/M	AG, SMG, PoCG, STG, MTG, ITG	Right	Seizure	Diffuse astrocytoma	Y/N	66	66	34	34	—

AG, angular gyrus; DNT, dysembryoplastic neuroepithelial tumor; IFG, inferior frontal gyrus; MEP, motor-evoked potential; MFG, middle frontal gyrus; MTG, middle temporal gyrus; PCL, paracentral lobule; PCu, precuneus; PoCG, postcentral gyrus; post, postoperative; PrCG, precentral gyrus; pre, preoperative; SFG, superior frontal gyrus; SMG, supramarginal gyrus; STG, superior temporal gyrus.

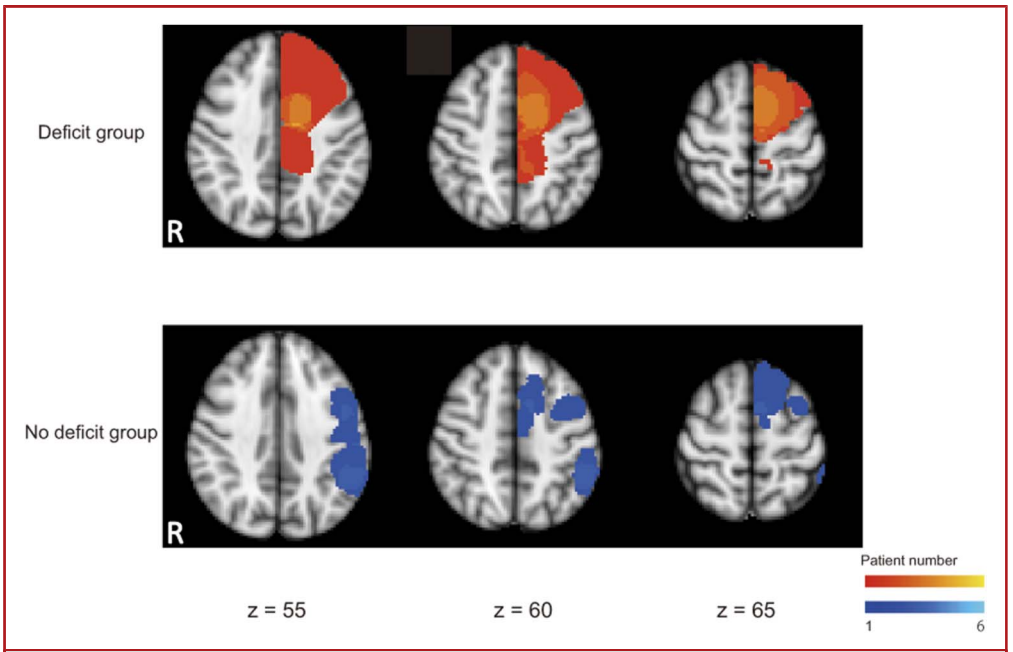

FIGURE 1. *Overlap of surgical resection in patients with additional postoperative motor deficit (Deficit group: 6 patients) and in patients without additional deficit (No deficit group: 6 patients). Color values represent the number of patients in whom a given area was resected. Orange regions were frequent in the deficit group whereas the light blue regions occurred frequently in the no deficit group. The data for 5 patients with the right hemispheric lesions are flipped to the left hemisphere. R, right.*

cortices. The protocol was approved by the local ethics committee, and all patients gave informed, written consent.

Experimental Design

Patients attended 2 sessions that involved the same protocols consisting of motor performance evaluation and MRI acquisition. The preoperative session was conducted within 6 months (mean, 40 days) before surgery. The postoperative session was performed within approximately 6 weeks (mean, 20 days) after surgery.

Motor performance was evaluated with the Fugl-Meyer assessment,[11] and the cases were divided into 2 groups. Six cases with additional postoperative motor deficits were classified into "deficit group," and 6 others without additional deficits were sorted into "no deficit group." At the time of 3-month postoperative visit in the deficit group, 3 cases fully recovered, and 3 cases represented mild motor deficits (1 with mild right hemiplegia, 1 with mild right leg weakness, and 1 with right hand clumsiness). Two right-handed cases in the deficit group (Cases 2 and 5) had transient postoperative speech impairment such as mutism.

Intraoperative Monitoring of Motor Function

Motor function was monitored by MEPs during surgery when available.[12] We regarded an MEP amplitude reduction of 50% or more as a warning sign of motor deficits.[1]

MRI Data Acquisition

MRI were acquired on a 3T Trio scanner (Siemens, Erlargen, Germany): T1-weighted anatomic images, BOLD fMRI, and DWI.[13-15]

During resting-state fMRI, subjects were instructed to maintain fixation on a white cross. The motor task fMRI paradigms were self-initiated movements at a rate about 1 Hz: (1) index finger to thumb opposition movement of the right hand and (2) left hand and (3) flexion and extension of the right ankle and (4) the left ankle.

Lesion Segmentation and Flip

Boundaries of surgical resection were manually determined on the T1-weighted image. We oriented all images such that the left side of the brain corresponded to the ipsilesional hemisphere. We therefore flipped the data of 5 patients with right hemispheric lesions (2 in the deficit group and 3 in the no deficit group) for further analyses.

The boundaries of surgical resection in T1-weighted images of individual subjects were transformed into the Montreal Neurological Institute (MNI) 152 2 mm template using a software from FMRIB Software Library (FSL 4.1.6; www.fmrib.ox.ac.uk/fsl).[14,16]

Mask Definition

For cortical structures, masks were specified in the primary motor area (M1), lateral PM, and medial PM in both ipsilesional and contralesional hemispheres by using Freesurfer (version 5.0.0; http://surfer.nmr.mgh.harvard.edu/). Subcortical masks were created in the white matter and ventricle with FMRIB's Automated Segmentation Tool.

fMRI Data Analysis

Functional data were analyzed using the FSL. In resting-state fMRI analysis, functional connectivity was computed using anatomic mask of ipsilesional M1.[17] Individual correlation maps were transformed from

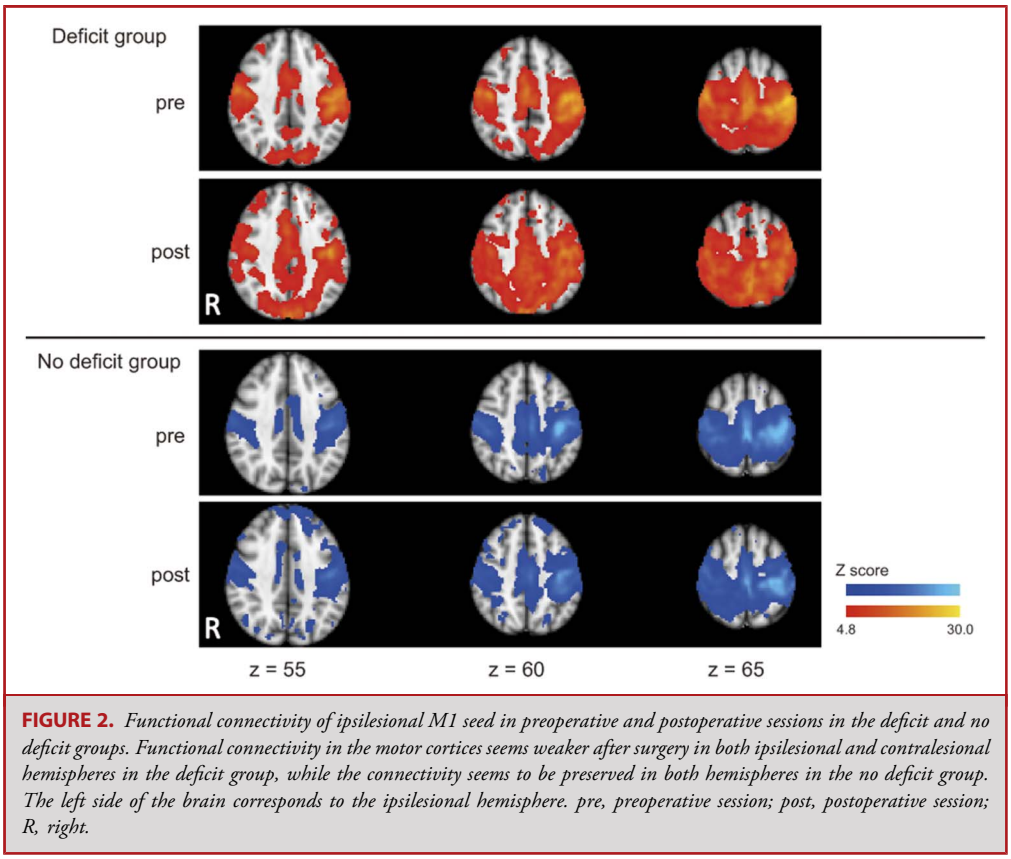

FIGURE 2. *Functional connectivity of ipsilesional M1 seed in preoperative and postoperative sessions in the deficit and no deficit groups. Functional connectivity in the motor cortices seems weaker after surgery in both ipsilesional and contralesional hemispheres in the deficit group, while the connectivity seems to be preserved in both hemispheres in the no deficit group. The left side of the brain corresponds to the ipsilesional hemisphere. pre, preoperative session; post, postoperative session; R, right.*

functional space into individual anatomic space, then into MNI 152 2 mm space. The MNI space correlation maps were submitted to a group general linear model analysis with a fixed-effects approach.

In the motor task fMRI, statistical maps for comparing the movement and rest were thresholded at $P < .05$ corrected (family-wise error corrected). Activated clusters were affine-transformed from functional space into individual T1-weighted space and entered into DWI data analysis.

DWI Data Analysis

DWI data were analyzed using FSL, as reported previously.[14] Masks for tractography were specified as an overlapping area between suprathreshold voxels in motor task fMRI and territory in M1 and lateral and medial PMs obtained from Freesurfer.

For corticofugal connectivity, probabilistic tractography was run from all voxels in the mask within the ipsilesional cerebral peduncle as the seed to reach each of the ipsilesional motor cortical masks (M1 and lateral and medial PMs) as the target.[18-20] We excluded indirect connections by discarding samples if they passed into the contralesional cortical motor areas or any of the other target masks before entering the target of interest. We also discarded samples if they passed into the lower brainstem corresponding to below z = 20 in the MNI space.[21] For cortico-cortical connectivity, tractography was computed from voxels in the ipsilesional M1 mask as the seed to voxels in the masks in ipsilesional lateral and medial PMs and contralesional M1 as the target. We excluded indirect connections by discarding samples if they passed into any of the other cortical motor target masks, the cerebral peduncle, striatum, or thalamus before entering the target of interest.

We chose 3 summary measures based on a previous study[22]: mean connectivity value, mean fractional anisotropy (FA) value, and total number of voxels of the fiber tracts. The mean connectivity value of the thresholded connectivity map was obtained for each subject and defined as the top quarter mean connectivity. The top quarter mean connectivity value, mean FA value, and the total number of voxels were submitted to repeated measures analysis of variance, with the groups as a between-subject factor and preoperative and postoperative sessions as a within-subject factor.

The details of Methods are shown in Supplemental Methods, http://links.lww.com/NEUOPEN/A52.

RESULTS

Intraoperative Monitoring

MEPs were measured during surgery in 5 cases in the deficit group and 4 in the no deficit group, and the amplitude was maintained within 50% decrease in all cases (Table 1). Awake craniotomy was performed in 5 cases in the deficit group and 4 cases in the no deficit group. The patients had deficits despite awake craniotomy because the dorsomedial frontal cortex was resected and SMA syndrome was suspected.[3] MEP or awake craniotomy was not conducted because of clinical grounds and technical problems.

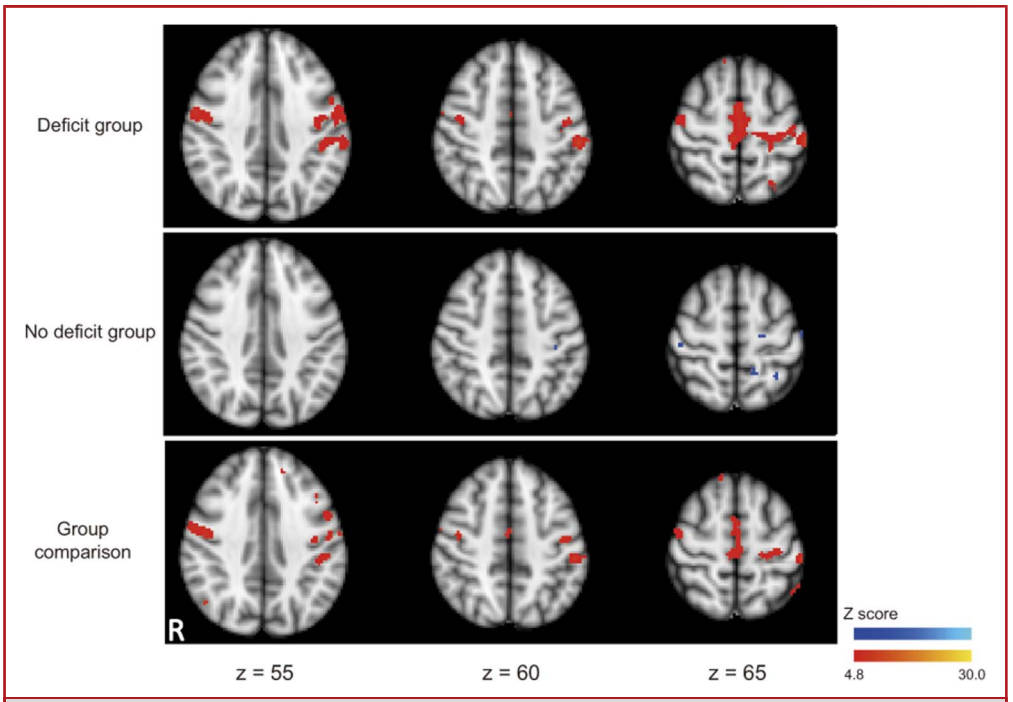

FIGURE 3. *Changes in functional connectivity of ipsilesional M1 seed after surgery in the deficit group, no deficit group, and group comparison. Functional connectivity decreased in the motor network in the deficit group while the decrease was only observed in limited areas in the no deficit group ($P < .05$, corrected). Group comparison demonstrated that the decrease in functional connectivity after surgery is greater in the motor network in the deficit group than in the no deficit group ($P < .05$, corrected).*

Lesion Mapping

Overlaying of the surgically resected area in the deficit group showed an area of overlap in the medial PM in all 6 patients, whereas the overlay in the no deficit group demonstrated areas of overlap in the medial PM in 3 patients and in the lateral PM or parietal region in 3 patients (Figure 1).

Functional Connectivity Analysis Using Resting-State fMRI

The correlation maps of resting-state activity were obtained in both groups ($P < .05$, corrected; Figure 2). Comparison of the maps between the preoperative and postoperative sessions revealed that the correlation in the motor cortices seems weaker in the deficit group while the correlation seems to be preserved in the no deficit group.

This visual impression was supported by a statistical evaluation because the correlation significantly decreased in the motor system in the deficit group while the decrease was observed only in limited areas in the no deficit group ($P < .05$, corrected; Figure 3 and Supplemental Table 1). Group comparisons demonstrated that the reduction in correlation after surgery was significantly greater in the deficit group than in the no deficit group ($P < .05$, corrected; Figure 3 and Supplemental Table 1, http://links.lww.com/NEUOPEN/A53).

Anatomic Connectivity Analysis Using DWI Tractography

The changes before and after surgery in the total number of voxels of M1 and lateral and medial PMs in the ipsilesional hemisphere showed no significant difference between the deficit group and the no deficit group in hand nor foot representation (Supplemental Table 2, http://links.lww.com/NEUOPEN/A54).

The changes before and after surgery in the top quarter mean connectivity values of the corticofugal tracts indicate that the connectivity values of the corticofugal tracts did not show significant differences between the groups. The changes before and after surgery in the mean FA values for the corticofugal tracts did not reach statistical significance between the groups. The total number of voxels of the corticofugal tracts showed no significant difference between the groups (Table 2).

The changes after surgery in the top quarter mean connectivity values of cortico-cortical tracts did not demonstrate significant differences between the groups, except those between M1 and lateral PM of the leg representation in the ipsilesional hemisphere. The changes after surgery in the mean FA values of the cortico-cortical tracts did not reach statistical significance between the groups. There were no significant differences between the groups in the changes after surgery in the total number of voxels of cortico-cortical tracts (Table 3).

TABLE 2. Corticofugal Tract From Ipsilesional Motor Cortical Areas

		Deficit group		No deficit group		Group × operation
	Corticofugal tract	Before surgery	After surgery	Before surgery	After surgery	*P*-value
Top quarter mean connectivity value						
Hand	M1	760 ± 140	724 ± 277	1055 ± 494	834 ± 619	.68
	Medial PM	111 ± 63	96 ± 117	250 ± 397	105 ± 64	.43
	Lateral PM	584 ± 394	383 ± 224	691 ± 420	457 ± 443	.91
Foot	M1	1045 ± 522	1199 ± 628	1724 ± 714	1353 ± 425	.22
	Medial PM	163 ± 141	139 ± 112	369 ± 354	405 ± 302	.76
	Lateral PM	168 ± 152	209 ± 175	260 ± 259	240 ± 288	.62
Mean FA value						
Hand	M1	0.51 ± 0.03	0.43 ± 0.08	0.48 ± 0.02	0.40 ± 0.20	.94
	Medial PM	0.45 ± 0.04	0.22 ± 0.25	0.43 ± 0.02	0.37 ± 0.11	.14
	Lateral PM	0.41 ± 0.21	0.34 ± 0.17	0.38 ± 0.19	0.29 ± 0.23	.89
Foot	M1	0.43 ± 0.22	0.50 ± 0.06	0.51 ± 0.06	0.49 ± 0.03	.37
	Medial PM	0.33 ± 0.26	0.30 ± 0.24	0.41 ± 0.21	0.45 ± 0.03	.68
	Lateral PM	0.32 ± 0.25	0.30 ± 0.24	0.42 ± 0.19	0.34 ± 0.26	.67
Total number of voxels						
Hand	M1	7611 ± 3279	5673 ± 1466	7691 ± 5322	6760 ± 7007	.57
	Medial PM	10 430 ± 7124	4448 ± 5222	9230 ± 4000	8813 ± 5800	.07
	Lateral PM	9573 ± 3406	5344 ± 2897	8860 ± 6614	6809 ± 6437	.20
Foot	M1	9244 ± 3055	9556 ± 4990	10 733 ± 6931	9466 ± 7023	.52
	Medial PM	7405 ± 5039	7752 ± 6884	7380 ± 4929	8913 ± 4508	.70
	Lateral PM	6160 ± 5337	5373 ± 5023	6866 ± 2590	2693 ± 2792	.30

FA, fractional anisotropy; M1, primary motor area; PM, premotor area.
Values are mean ± SD.

A part of Results is shown in Supplemental Results, http://links.lww.com/NEUOPEN/A55.

DISCUSSION

Temporally coherent network activity among M1 and lateral and medial PMs during resting-state fMRI was significantly reduced in the postoperative session in patients with additional postoperative motor deficit. The surgically resected area is unlikely to fully explain the additional motor deficit because the resection in similar areas was observed in both groups. Similarly, the additional motor deficit is unlikely to be attributable to surgical resection of specific anatomic connectivities among the motor cortical areas because the present findings suggest that the disruption of the estimated cortico-cortical fiber tract due to tumor removal was not necessarily different in both groups. The intraoperative observations agree with imaging findings suggesting preserved anatomic connectivity of the estimated corticofugal fiber tract. Taken together, the present findings suggest that the postoperative motor deficit that arises from discrete brain lesions is linked to the effects of the lesion on the reduction of functional connectivity organizing motor network.

Based on the surgically resected area in the dorsomedial frontal cortex in all 6 patients in the deficit group and 3 of 6 patients in the no deficit group, SMA syndrome was suspected in the deficit group. This interpretation was supported by follow-up observation at 3 months after surgery representing mild motor deficits in 3 of 9 cases (33.3%) because the outcome was similar level as supposed to occur in SMA syndrome (20.3%).[3] The present

TABLE 3. Cortico-Cortical Tract From Ipsilesional M1

		Deficit group		No deficit group		Group × operation
	Cortico-cortical tract	Before surgery	After surgery	Before surgery	After surgery	*P*-value
Top quarter mean connectivity value						
Hand	M1-M1	163 ± 368	53 ± 50	134 ± 329	257 ± 450	.16
	M1-medial PM	269 ± 178	42 ± 54	348 ± 558	538 ± 788	.13
	M1-lateral PM	27 089 ± 4162	19 676 ± 11 071	24 956 ± 6515	22 057 ± 12 327	.64
Foot	M1-M1	11 621 ± 10 134	3134 ± 3564	17 070 ± 11 108	13 218 ± 12 127	.57
	M1-medial PM	2469 ± 2252	887 ± 1073	3784 ± 2477	1784 ± 4082	.32
	M1-lateral PM	4126 ± 3368	998 ± 3541	5183 ± 3445	3372 ± 3821	.02
Mean FA value						
Hand	M1-M1	0.15 ± 0.23	0.07 ± 0.17	0.06 ± 0.15	0.13 ± 0.20	.35
	M1-medial PM	0.28 ± 0.11	0.16 ± 0.18	0.25 ± 0.14	0.25 ± 0.13	.19
	M1-lateral PM	0.22 ± 0.04	0.15 ± 0.08	0.22 ± 0.07	0.14 ± 0.08	.95
Foot	M1-M1	0.30 ± 0.23	0.18 ± 0.23	0.41 ± 0.05	0.44 ± 0.05	.94
	M1-medial PM	0.12 ± 0.10	0.14 ± 0.18	0.20 ± 0.11	0.21 ± 0.04	.05
	M1-lateral PM	0.12 ± 0.14	0.18 ± 0.11	0.13 ± 0.10	0.09 ± 0.11	.89
Total number of voxels						
Hand	M1-M1	7848 ± 9755	3308 ± 2439	3139 ± 6561	3836 ± 5126	.28
	M1-medial PM	4940 ± 2022	3303 ± 3947	4907 ± 2496	4226 ± 3438	.67
	M1-lateral PM	11 540 ± 3300	10 072 ± 9278	17 851 ± 10 781	13 023 ± 16 425	.45
Foot	M1-M1	12 919 ± 5869	10 677 ± 3338	13 677 ± 3808	12 832 ± 5215	.68
	M1-medial PM	3725 ± 2333	5117 ± 5000	7929 ± 6337	7279 ± 3469	.41
	M1-lateral PM	3402 ± 2648	9225 ± 9546	6865 ± 8202	5010 ± 9983	.05

FA, fractional anisotropy; M1, primary motor area; PM, premotor area.
Values are mean ± SD.
Cortico-cortical tract between ipsilesional motor cortical areas and between ipsilesional and contralesional M1-M1.

findings suggest that SMA syndrome is caused by disorganization of functional connectivity among cortical motor networks rather than by resection of anatomic connectivity of the corticofugal pathway. The present findings propose an idea that monitoring motor network between cortices such as cortico-cortical–evoked potentials[13,15,23-25] might be useful to prevent SMA syndrome.

The present findings support the notion that motor control of the cerebral cortex requires functional connectivity constituted of a modular community structure. The boundaries of the spatially distributed functional connectivity generally agree with brain areas involved in motor control. A previous study demonstrated that temporally coherent functional connectivity among brain areas can be disorganized in the absence of anatomic damage to each region or their physical linkage.[26] Similarly, disruption of functional connectivity in this study was not attributable only to damage to the specific cortical region or the cortico-cortical connection. The key factors maintaining motor behavior and integrity of functional connectivity should be clarified in future studies.

Previous clinical studies also reported that some patients with premotor lesions demonstrate motor deficits, while others do not.[27,28] The present findings propose that premotor lesions lead to motor deficits when the system level of the motor network is damaged. The PMs organize strong, reciprocal anatomic connections with M1, suggesting that PM and M1 act in concert to control movement.[29,30] In addition, each PMs and M1 individually forms unique anatomic connections with prefrontal and posterior parietal cortices[31] and with the basal ganglia and cerebellum,[32,33] implying that each area operates complementary motor commands. Thus, premotor lesions can result

in disruption of information exchange for motor control across different brain areas, leading to motor deficits.

As an alternative hypothesis, one may argue that damage to the corticofugal axons causes postoperative motor deficits. The main corticospinal projections underlying the MEP are likely to be large thickly myelinated axons from M1[2] and axons from PMs that also send direct projections to the spinal cord[34] may be difficult to monitor. Thus, it might be possible to argue that damage to the corticospinal axons especially from lateral and/or medial PMs causes the motor deficits. However, this argument is inconsistent with the present imaging findings suggesting that damage to the anatomic connectivity of the estimated corticofugal fiber tract was unlikely to lead to postoperative impairments. In addition, this argument is difficult to reconcile with the present imaging findings demonstrating the reduction in functional connectivity measured with fMRI signals in patients with postoperative deficits. This is because if axonal damage causes the deficits, output failure is important for functional consequences and cortical neuronal loss is typically modest.[35,36] Neuronal inputs to the motor cortices, therefore, should be maintained, and patients with and without postoperative deficits should show similar levels of local field potential as well as BOLD fMRI signals in the motor network.[37,38]

Analyses of the cortico-cortical fiber tract showed a greater increase in the total number of tract voxels and a greater decrease in top quarter mean connectivity values in the postoperative session in patients with additional deficits in ipsilesional M1-lateral PM tract of leg representation. Thus, a larger ipsilesional M1-lateral PM anatomic tract was delineated, and smaller connectivity value was measured after surgery in patients with postoperative deficits. These findings suggest that the ipsilesional M1-lateral PM fiber tract expanded and fiber density decreased in patients with postoperative deficits. Thus, the present findings suggest disruption of the estimated cortico-cortical fiber tracts due to tumor removal was not necessarily greater in patients with additional postoperative deficits.

Limitations

There were several limitations in this study. First, the number of participants was small, and their backgrounds were heterogeneous including high-grade and low-grade gliomas and tumor locations. Second, 3 cases in the deficit group fully recovered at 3 months after surgery although follow-up fMRI after recovery was not obtained.

CONCLUSION

The present findings suggest that motor deficits developing after medial PM resection or SMA syndrome are related to disorganized cortical motor networks rather than resection of anatomic connectivity of corticofugal pathway. This idea opens up new perspectives for new diagnostic and rehabilitation methodologies for patients with SMA syndrome. Future studies will help clarify the key factors connecting behavioral performance and the integrity of functional connectivity.

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Disclosures

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Supplemental Methods. Additional details about the procedure.
Supplemental Results. Additional details about the result.
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