의학박사 학위논문

운동 및 감각 뇌기능 영역 절제 후 신경학적 결과에 대한 국소 해부학적 분석

- 주변 영역 추가 절제의 영향 –

Topographical analysis of neurological outcome following motor and sensory area resection

- Implication of additional resection of adjacent area -

2017 년 01 월

서울대학교 대학원
의학과 뇌신경과학 전공
김 영 훈

A thesis of the Degree of Doctor of Philosophy

운동 및 감각 뇌기능 영역 절제 후 신경학적 결과에 대한 국소 해부학적 분석

- 주변 영역 추가 절제의 영향 -

지도교수 정 천 기

이 논문을 김영훈 박사 학위 논문으로 제출함

2016 년 10 월

서울대학교 대학원

의학과 뇌신경과학 전공

김 영 훈

김영훈의 박사 학위 논문을 인준함

2017 년 01 월

위 원 장 권 준 수 (인)

부위원장 정 천 기 (인)

심사위원 손 철 호 (인)

심사위원 김 재 용 (인)

심사위원 김 정 훈 (인)

ABSTRACT

Topographical analysis of neurological outcome following motor and sensory area resection

- Implication of additional resection of adjacent area -

Young-Hoon Kim

Department of Neurosurgery

The Graduate School, Seoul National University

Introduction

The resection of the motor and somatosensory area (MSA) has been challenging due to the postoperative neurological deficits. The author hypothesized that the additional resection of the adjacent area of the motor and MSA could increase the postoperative neurological risk. This study was designed to evaluate the neurological deterioration that follows the MSA resections and to assess the topographical risk factors associated with these morbidities.

Materials and Methods

The author reviewed 109 consecutive patients who suffered from medically intractable epilepsy and underwent the resection of the MSA and / or adjacent area under awake anesthesia. The cohort included the 33 patients with primary motor cortex (PMC) resection, 43 patients with supplementary motor area

(SMA) resection, and 24 patients with primary sensory cortex (PSC) resection. The etiological diagnoses were brain neoplasm in 54 patients (49.5%), cortical lesion in 25 (22.9%), and no lesion in 30 (27.5%). All topographical analyses of the resected area were performed based upon pre- and post-operative magnetic resonance images.

Results

After the PMC resection, 67% of the patients experienced neurological worsening including 15% of the permanent deficits. The postoperative neurological worsening was not significantly associated with the additional adjacent area resection, but with the specific location (e.g., posterior upper quadrant) of the resected area of the PMC. The SMA syndrome occurred in the 47% of the patients who underwent SMA resection, and this was significantly associated with the additional resection of the cingulate gyrus. The neurological risk of the PSC resection was 40%. The additional resection of the posterior parietal cortex (PPC) was the significant risk factor for the development of postoperative neurological impairments.

Conclusion

After the resection of the MSA and its adjacent area, 48% of the patients experienced neurological impairments including 9% of the permanent deficits. The additional resection of the cingulate gyrus and the PPC increased significantly the postoperative neurological risk after the SMA and PSC resection, respectively. The results imply that the neurological outcome after

the resection of the MSA may be influenced by the disruption of the network between the eloquent and its adjacent area rather than the damage of the only eloquent area.

Keywords: primary motor cortex, primary sensory cortex, supplementary motor area, cingulate gyrus, posterior parietal cortex

CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

The primary motor and somatosensory area (MSA), which is traditionally equivalent to the same area as the Brodmann's area 1, 2, 3, and 4, had been considered to be an unresectable region because of the potential for neurological morbidity.[17, 22] Motor weakness or paralysis, facial palsy, or dysarthria can occur after the resection of the primary motor cortex (PMC). The resection or injury of the primary somatosensory cortex (PSC) can lead not only to sensory impairments such as paresthesia, astereognosia, and proprioceptive sensory loss, but also to apraxia and motor deficits.

In 1886, Victor Horsley firstly resected and area of posttraumatic central cortical lesion in a 22-year-old man by using stimulation mapping with application of general anesthesia.[5] Pilcher et al. performed the largest corticectomy series involving portions of the MSA by using cortical stimulation mapping after administration of local anesthesia in 1947. They reported that the rate of permanent neurological deficits was 63% after even the partial sensori-motor cortical resections in 41 patients with Jacksonian convulsions.[22] Pilcher et al. therefore demonstrated that an favorable return of motor function was possible following limited resections involving the MSA.[22]

Recent advancements, however, in magnetic resonance imaging (MRI), functional MRI, awake anaesthesia, and intraoperative mapping and monitoring technologies have gradually enabled surgeons to remove the primary MSA with acceptable neurological morbidities.[11] In actuality, many

authors have reported satisfactory results after the resection of the Rolandic area for controlling medically intractable epilepsy or for removing tumorous lesions.[2, 5, 7, 11, 16, 23, 28] Based on previous reports, postoperative new neurological deficits were mostly transient or mild, and the rate of permanent neurological morbidities was acceptable, ranging from 0 to 50%.[2, 5, 7, 11, 16, 23, 28]

However, the postoperative neurological status of the patients who underwent a resection of the MSA was too variable, from no neurological symptoms to permanent hemiparesis or language deficits. The literature contains conflicting results as regards the neurological results after the resection of those areas, with some authors reporting favorable results and others persistent impairments. The reported series showed both cautionary and reassuring evidence with regard to the neurological outcome after the resection of the MSA. [1, 2, 5, 11, 13, 14, 22, 23]

In many previous studies there was uncertainty concerning the precise boundaries for safe MSA resection and the depth of the resection into the underlying white matter. In addition, no definite causative factors have been demonstrated after the resection, and the implication of the resected area and depth to the postoperative neurological outcome has been unknown.[11, 14] Thus, the neurological outcome of limited cortical resection in the MSA in humans remains poorly described.

Therefore, this study was designed to demonstrate the possible mechanism of the variability of the postoperative neurological sequelae following the MSA resection. The author focused on the implication of the adjacent non-eloquent area and hypothesized that the additional resection of the adjacent

area of the MSA could increase the postoperative neurological risk. The hypothesis began with a presumption that the postoperative neurological outcomes and deficits were influenced by not the damage of the only eloquent center (e.g. PMC or PSC), but the disruption of the neurophysiological connections between the eloquent area and its adjacent non-eloquent areas or the total amount of damage of both these two areas. Therefore the author focused on the additional resection or damage of the adjacent area including the premotor area, cingulate gyrus, or posterior parietal cortex (PPC).

This study was finally performed to assess the postoperative neurological outcomes following the resection of MSA including PMC, PSC, and supplementary motor area (SMA) and to demonstrate topographical risk factors for these deficits, focusing on the implication of the additional resection of the adjacent area of the MSA.

MATERIALS AND METHODS

Patients

A total of 187 consecutive patients who had epileptogenic focus or tumorous lesion in the eloquent area or its adjacent areas underwent the surgical resection under awake anesthesia between 1994 and 2012 in our institutions. Inclusion criteria were as follows: (1) resection of the primary MSA and its adjacent areas, (2) available pre- and post-operative MRIs, and (3) clinical follow-up over 2 years. All the patients underwent a surgery under awake anaesthesia with intraoperative monitoring. The primary MSA was the same area as the precentral and postcentral gyrus. The precentral gyrus was limited anteriorly by the precentral sulcus, posteriorly by the central sulcus, medially by the cingulate sulcus, and laterally by the sylvian fissure. The postcentral gyrus was limited anteriorly by the central sulcus, posteriorly by the post-central sulcus, medially by the cingulate sulcus, and laterally by the sylvian fissure. Fifty-eight patients who did not undergo the resections of the MSA, but other areas including the Broca's, Wernicke's and deeper white matter areas were excluded in the present study. We excluded 7 patients without pre- or post-operative MRIs and 13 patients due to follow-up loss before 2 years postoperatively. (Figure 1) Finally, a total of 109 consecutive patients who underwent the surgical resection of the MSA and / or its adjacent gyrus for pharmacologically intractable epilepsy were enrolled and retrospectively reviewed in this study (Table 1).

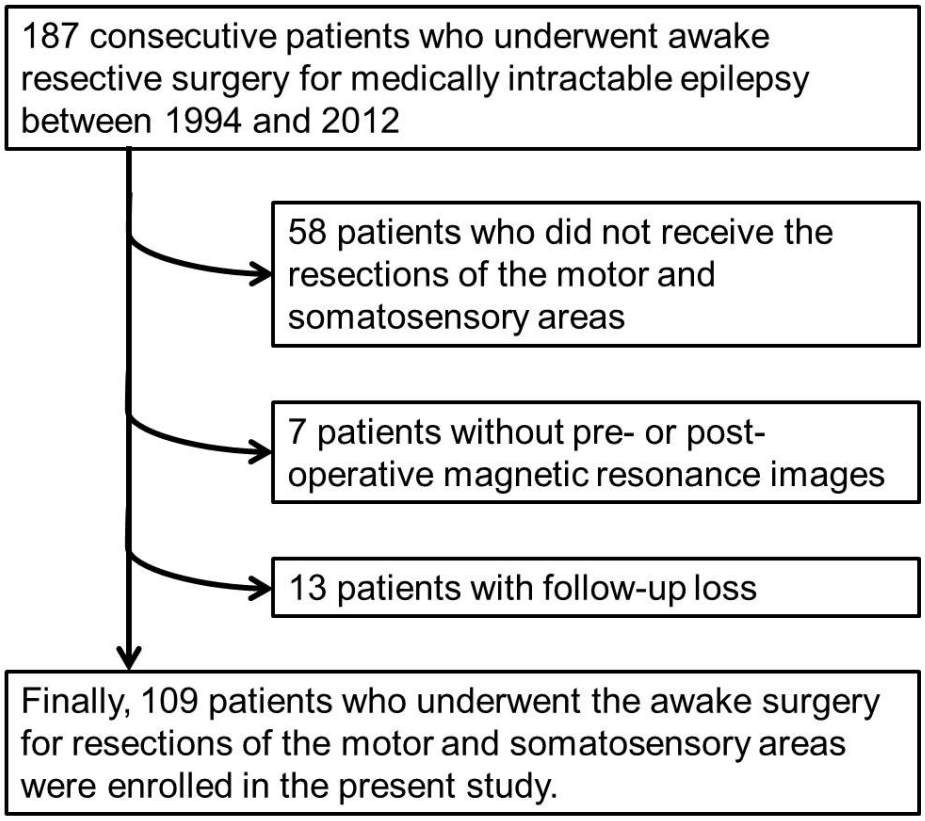


Figure 1

Diagram of the selection of the enrolled patients in the present study

Table 1

Demographic and radiological data of the 109 patients who underwent the resection of the motor and sensory area and / or its adjacent cortices

Parameters	Values*
Male Sex	62 (56.9%)
Age	33.0 ± 12.0 (15 – 63)
Type of seizures	
Simple partial seizures	24 (22.0%)
Complex partial seizures (CPS)	18 (16.5%)
CPS with secondary generalization	35 (32.1%)
Generalized tonic-clonic seizures	28 (25.7%)
Others	4 (3.7%)
Duration of seizures (years)	8.8 ± 8.0 (0.0 – 30.0)
Frequency of seizures (/month)	14.8 ± 37.8 (0.0 – 300.0)
Predisposing factors	
Head trauma	15 (13.8%)
CNS infection	6 (5.5%)
Febrile seizure	7 (6.4%)
Developmental anomaly	3 (2.8%)
No	78 (71.6%)
Number of preoperative AED	
1	35 (32.1%)
2	37 (33.9%)
3	21 (19.3%)
≥ 4	16 (14.7%)
Preoperative neurological deficits	25 (22.9%)

Preoperative MRI findings	
Tumorous lesion	54 (49.5%)
Cortical lesion	25 (22.9%)
No lesion	30 (27.5%)

* Values are expressed as number (percentage) or mean values ± standard deviation (range).

CNS, central nervous system; AED, anti-epileptic drug; MRI, magnetic resonance imaging

Sixty-two patients (56.9%) were male, and 47 patients (43.1%) were female. The mean patient age was 33.0 ± 12.0 years (range, 15 – 63 years). The mean length of seizure history and frequency were 8.8 ± 8.0 years and 14.8 ± 37.8 / month, respectively. Twenty-five patients (22.9%) had neurological deficits preoperatively. Tumorous lesions were found in 54 patients (49.5%) and cortical lesions in 25 patients (22.9%) in preoperative magnetic resonance imaging (MRI). Thirty patients (27.5%) showed no definite lesions on the preoperative MRI. The Institutional Review Board of the authors' institutions granted a waiver for informed consent and approved the present study.

Preoperative evaluations

The preoperative evaluation protocol included a routine history taking, physical and neurological examinations, prolonged interictal electroencephalography (EEG), ictal video-EEG monitoring (at least three usual seizures), brain MR imaging, positron emission tomography (PET) and interictal and ictal single-photon emission computed tomography (SPECT). The purpose of these preoperative studies was to localize an ictal onset zone, and the concordance of these studies enabled approximation of the epileptogenic zone. Additional functional evaluation included a Wada test, neuropsychological testing, functional MRI and magnetoencephalography (MEG), which were performed in selected patients. Subdural electrodes were implanted near the ictal onset zone according to video-EEG monitoring results, as no definite lesion was apparent on the MR images of all patients. All the

procedures for the insertion of the subdural electrodes were carried out under general anaesthesia. After implantation of the electrodes, video-EEG monitoring was performed until at least three typical seizures occurred. After the ictal onset zone was delineated, preoperative functional mapping (e.g., motor, sensory, and language functions) was carried out via stimulation of the subdural electrodes.

Surgical procedures

Surgical resection was performed on patients under awake anaesthesia with intraoperative cortical mapping and monitoring.[11-13] In the operating room, we took several points into consideration regarding patient positioning, which included neck comfort, transparent facial drape for continuous monitoring and access to the airway in case emergency intubation was required. A scalp nerve block was performed via the supra-orbital nerve, supratrochlear nerve, auriculotemporal nerve, zygomaticotemporal nerve, greater auricular nerve and occipital nerve, using local anaesthetics that included a combination of 0.5% bupivacaine and epinephrine (1:200,000). Simultaneously, the same anaesthetics were injected around the expected pin sites, and the Mayfield head fixator was applied. No intravenous sedative agent (e.g., propofol) was administered until the end of the functional mapping and resection of whole regions of the target, to avoid patient confusion. After the dura was opened, the location of the resection target was confirmed via the previously implanted subdural electrode and the stereotactic navigation system using the

imaging probe. Standard cortical mapping was performed using an Ojemann stimulator, which is a constant current generator that produces a train of biphasic square wave pulses (at a rate of 60 Hz, 1 msec / phase) to minimise the possibility of inducing a seizure. To locate the primary MSA, stimuli were applied in 1 mA increments, starting at 1 mA up to a maximum of 10 mA.[3] A surface EEG strip was used both to ensure a stimulation artefact and to perform observations after discharges. The neurologist or neurosurgeon monitored the patient during the cortical stimulation. (Figure 2A and 2B) Cortical areas that yielded a response on testing were labelled with small numbered paper tickets. After cortical stimulation, we performed a corticectomy that avoided all sites identified as the eloquent cortex. Whole resection of the target was carried out, during which neurological function (e.g., motor function of the contralateral upper and lower limbs and expressive and comprehensive function) was continuously monitored. The resection continued until either the epileptogenic zone was removed or the onset of neurological deficits occurred.

Postoperative evaluation and topographical analysis

Postoperative seizure outcomes and the neurological status of each patient were assessed at regular clinical follow-ups, which were scheduled at one month after the surgery and subsequently every two or three months. Each assessment was completed by the same neurologist and neurosurgeon. Seizure outcomes were assessed according to the Engel classification.[8]

(A)

(B)

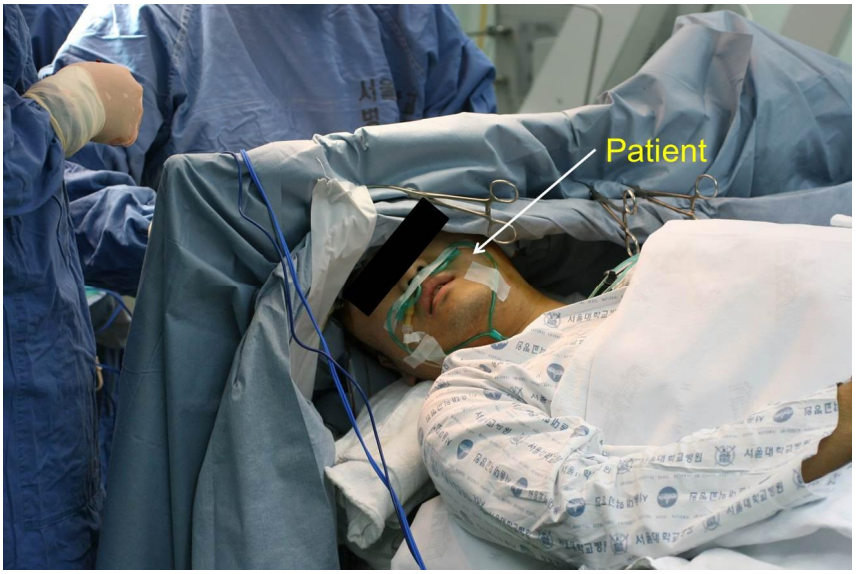
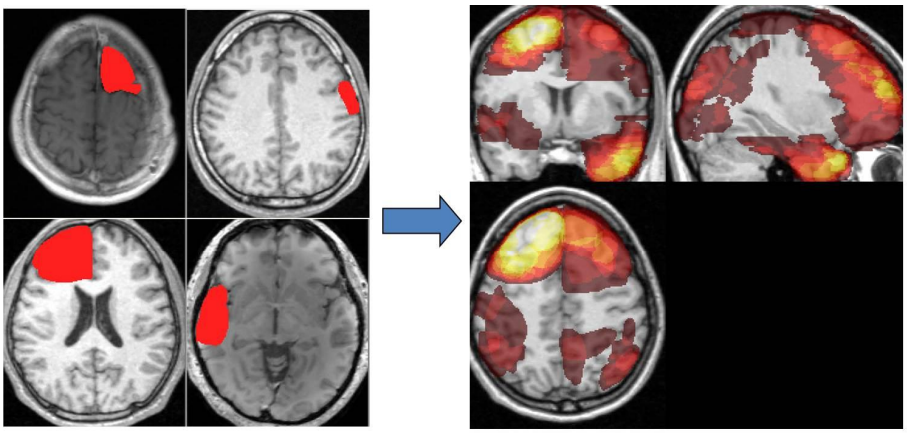


Figure 2

The pictures depict a resective surgery under awake anesthesia. A neurologist (A) monitored continuously the motor and language functions of a patient (B) during the cortical stimulation and resective procedure. (EEG; electroencephalograph, ECoG; electrocorgicogram)

A postoperative MRI was completed 3 months after surgery to measure the resected area. All the preoperative and postoperative images were spatially normalized using the Montreal Neurological Institute (MNI) atlas and the SPM5 software (available at http://www.fil.ion.ucl.ac.uk/spm/software/spm5) of Matlab 7.0 (MathWorks, Natick, Mass.). All resected areas (i.e., regions of interest or ROIs) were delineated manually on each preoperative MRI by comparison with each postoperative MRI using the MRIcro software (available at http://www.sph.sc.edu/comd/rorden/mricro.html). In this study, the preoperative MRI was used as the template to minimize the distortion of the postoperative MRI. We generated the resection frequency map by combining all ROIs together on an atlas using Matlab 7.0. As a result, two-dimensional axial, coronal and sagittal images and three-dimensional (3D) volume-rendering images were obtained using the MRIcron software (available at http://www.sph.sc.edu/comd/rorden/mricron). (Figure 3A and 3B) Based on the resection map of the postoperative MRIs, the resection of the PMC was performed in 33 patients, the PSC in 24 patients, the SMA in 43 patients, and the PPC in 34 patients. Ten patients underwent the resection of both the PMC and PSC, 6 patients both the PMC and SMA, 9 patients both the PSC and PPC, and 1 patient the PSC, PPC, and SMA. In this study, the neurological risk analysis was separately conducted in the each resection group of the PMC, PSC, and SMA to avoid confounding factors of several eloquent motor sensory areas.

(A)



(B)

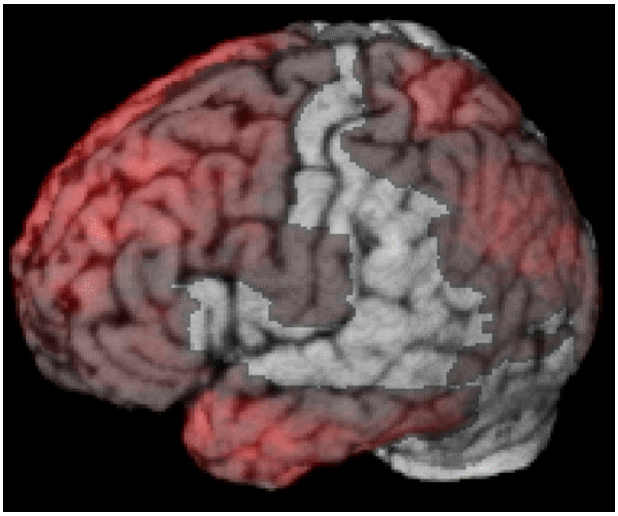


Figure 3

(A) All resected areas were delineated manually on each preoperative MRI by comparison with each postoperative MRI. The resection map was generated by combining all regions together on an atlas. As a result, two-dimensional axial, coronal and sagittal images and (B) three-dimensional volume-rendering images were obtained.

Several demographic and clinical factors including patient sex, age, seizure duration, seizure frequency, seizure type, presence of predisposing factors of seizures, presence of preoperative neurological deficits, preoperative MRI findings, side of surgery, surgery type, presence of intraoperative seizures, topographical resected area, total volume of the resected area, amount of time required for surgical resection, histological type, and seizure outcomes were evaluated via risk factor analysis for the development of postoperative neurological deficits.

Statistical analysis

All data are presented as the mean value ± standard deviation in addition to the range. The risk factors for developing postoperative neurological deficits were analysed using logistic regression analysis. To reduce the risk of Type II errors due to modest sample size, variables were considered for multivariate analysis only if they were associated with a dependent variable in each analysis that was significant at the $p < 0.25$ level. *P*-values of < 0.05 were considered statistically significant. All statistical analyses were performed using SPSS (version 22.0., 2013; SPSS, Chicago, IL, USA).

RESULTS

Overall surgical outcome

To delineate the ictal onset zone and eloquent cortices, the pre-resective subdural grid and electrode implantation was performed in 53 patients (48.6%). Resective surgeries included 58 lesionectomies (53.2%) and 51 corticectomies (46.8%). The mean operation time and postoperative hospital stay were 290.6 ± 77.8 minutes (range, 110 – 675) and 7.9 ± 5.8 days (range, 3 – 48), respectively. Histopathological examinations revealed 50 (45.9%) cortical dysplasias, 46 (42.2%) astrocytic tumours, 8 (7.3%) vascular lesions, and 5 (4.6%) others.

At the last follow-up evaluation for seizure outcome, 56 patients (51.4%) were found to have achieved Engel's class I (seizure-free), 20 patients (18.3%) achieved class II (rare seizures), and 21 patients (19.3%) achieved class III (worthwhile improvement). The seizure control rate was 69.7% (Engel's class I and II). During follow-up duration, 25 patients (22.9%) was able to stop the anti-epileptic drugs (AED) and 32 patients (29.4%) to decrease the numbers or amount of AED. The mean time elapsed from surgery to final clinical follow-up was 90.0 ± 61.1 months (range, 12 – 251 months). The surgical results are summarised in Table 2.

Table 2

Operative results and neurological outcome of the 109 patients who underwent the resection of the motor and sensory area and / or its adjacent cortices

Parameters	Values*
Pre-resective subdural grid implantation	53 (48.6%)
Type of surgery	
Lesionectomy	58 (53.2%)
Corticectomy	51 (46.8%)
Side of surgery	
Right	44 (40.4%)
Left	65 (59.6%)
Resected area	
Primary motor cortex (PMC) only	17 (15.6%)
Primary sensory cortex (PSC) only	4 (3.7%)
Supplementary motor area (SMA) only	38 (34.9%)
Posterior parietal cortex (PPC) only	24 (22.0%)
Both PMC and PSC	10 (9.2%)
Both PMC and SMA	6 (5.5%)
Both PSC and PPC	9 (8.3%)
Both PSC, PPC, and SMA	1 (0.9%)
Operation time (minutes)	290.6 ± 77.8 (110 – 675)
Postoperative hospital stay (days)	7.9 ± 5.8 (3 – 48)
Pathological examinations	
Cortical dysplasia	50 (45.9%)
Brain tumors	46 (42.2%)
Vascular lesions	8 (7.3%)

Others	5 (4.6%)
Postoperative neurological deficits	
Permanent	10 (9.2%)
Transient	42 (38.5%)
No	57 (52.3%)
Seizure outcome at last f/u (Engel's classification)	
I	56 (51.4%)
II	20 (18.3%)
III	21 (19.3%)
IV	12 (11.0%)
Postoperative AED at last f/u	
Decrease number or amount	32 (29.4%)
Discontinuation	25 (22.9%)
No change	52 (47.7%)
Clinical f/u duration (months)	90.0 ± 61.1 (12 – 251)

* Values are expressed as number (percentage) or mean values ± standard deviation (range).

AED, anti-epileptic drug; f/u, follow-up

Neurological outcome after the primary motor cortex resection

Of the 33 patients (Table 3) with the PMC resection, 22 patients (66.7%) experienced new and postoperative neurological deficits. Five of these patients experienced permanent deficits (15.2%), and 17 experienced transient deficits (51.5%). The permanent deficits were composed of 2 contralateral instances of weakness, 1 fine movement disturbance of the hand, 1 sensory disturbance including hypaesthesia and dysesthesia, and 1 mild dysarthria. Transient deficits included contralateral motor weakness in 10 patients, facial palsy in 3 patients, motor dysphasia in 6 patients, and dysarthria in 1 patient. (Table 4) Of the 17 patients with transient deficits, 12 patients (70.6%) fully recovered within 3 months. The mean recovery time was 84.1 ± 81.2 days (range, 3 – 300 days).

Of the 33 patients, 8 patients underwent the resection of the PMC only, 6 patients both the PMC and SMA, 9 patients both the PMC and other frontal lobe area including the premotor areas, and 10 patients both the PMC and PSC. The neurological risk of the 6 patients with the resection of both the PMC and SMA (100.0% 6/6) was higher than those of the 8 patients with the PMC only (75.0%, 6/8), the 9 patients with the PMC and the premotor areas (44%, 4/9), and the 10 patients with both the PMC and PSC (60.0%, 6/10); but this was not statistically significant ($p = 0.249$). (Table 5)

However, the neurological risk after the PMC resection was associated with the location of the resected area in the PMC rather than the additional resection of the adjacent area to the PMC. The author categorized the PMC

Table 3

Clinical findings of the 33 patients following primary motor cortex resection

No	Sex/ Age	Neurological deficits	Recovery (days)	Resected Area (AP)	Resected area (UL)
1	F/19	wrist & hand weakness (Gr 3)	21	P	U
2	M/32	UE weakness (Gr 3)	12	P	UM
3	M/34	UE & LE weakness (Gr 3), motor dysphasia	150	P	M
4	F/43	UE & LE weakness (Gr 4)	permanent	A	U
5	M/17	-	-	P	L
6	M/24	mild dysarthria, facial palsy	permanent	P	L
7	M/45	UE & LE weakness (Gr 2)	30	A	U
8	M/34	-	-	P	L
9	F/34	motor dysphasia	180	A	ML
10	M/44	motor dysphasia	3	A	L
11	F/60	-	-	A	L
12	M/16	-	-	A	L
13	F/31	facial palsy	60	A	M
14	M/54	motor dysphasia	300	P	L
15	M/40	UE weakness (Gr 4), motor dysphasia	6	A	UM
16	M/35	motor dysphasia, facial palsy	180	P	M
17	F/30	-	-	P	L
18	F/51	fine movement disturbance of hand	permanent	P	M

19	M/35	hand hypesthesia & dysesthesia	permanent	P	M
20	M/58	-	-	A	L
21	M/48	UE weakness (Gr 4)	30	P	U
22	M/60	UE weakness (Gr 4)	90	A	U
23	F/41	facial palsy	90	P	L
24	F/19	ankle weakness (Gr 3)	120	P	L
25	M/48	-	-	A	M
26	F/42	-	-	A	U
27	F/36	-	-	A	L
28	F/61	dysarthria	7	P	L
29	M/25	hand weakness (Gr 3)	90	P	M
30	F/20	-	-	A	M
31	M/63	UE weakness (Gr 3)	permanent	P	M
32	F/59	hand weakness (Gr 3)	60	P	M
33	M/61	-	-	A	M

No, number; AP, antero-posterior location of the resected area; UL, upper-lower location of the resected area; F, female; M, male; Gr, grade; UE, upper extremity; LE, lower extremity; A, anterior PGR; P, posterior PGR; U, upper third PGR; M, middle third PGR; L, lower third PGR

Table 4

Postoperative neurological risk following the resection of the primary motor cortex (n = 33)

Parameters	Values
Overall neurological deficits	22 (66.7%)
Permanent deficits	5 (15.2%)
Contralateral weakness	2
Dysarthria	1
Dysesthesia	1
Fine movement disorder	1
Transient deficits	17 (51.5%)
Contralateral weakness	10
Dysarthria or dysphasia	7
Facial palsy	3

Table 5

Postoperative neurological risk analysis according to the topographical resected area based on the postoperative magnetic resonance image in the 33 patients with the resection of the primary motor cortex

Resected area	Transient ND	Permanent ND	Total ND
PMC only (n=8)	5 (62.5%)	1 (12.5%)	6 (75.0%)
PMC and SMA (n=6)	5 (83.3%)	1 (16.7%)	6 (100.0%)
PMC and premotor area (n=9)	4 (44.4%)	0 (0.0%)	4 (44.4%)
PMC and PSC (n=10)	3 (30.0%)	3 (30.0%)	6 (60.0%)
Total (n=33)	17 (51.5%)	5 (15.2%)	22 (66.7%)

PMC, primary motor cortex; SMA, supplementary motor area; PSC, primary somatosensory cortex; ND, neurological deficits

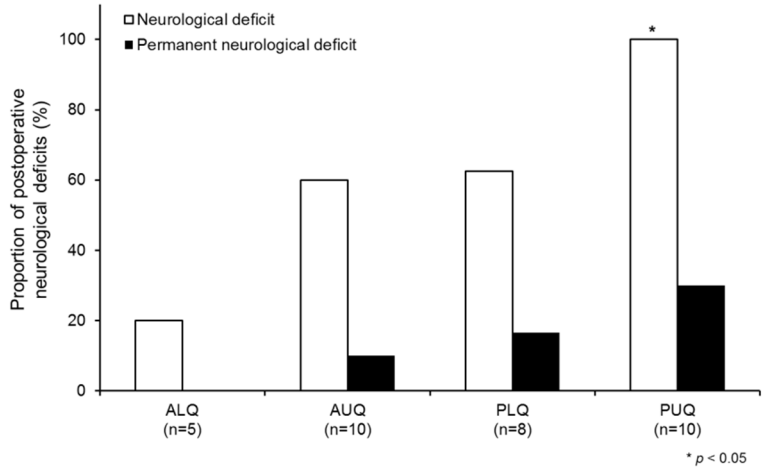
resection into 4 quadrant resections: the anterior upper quadrant (AUQ), the posterior upper quadrant (PUQ), the anterior lower quadrant (ALQ), and the posterior lower quadrant (PLQ) PMC resection.

All 10 patients who underwent resection of the PUQ PMC experienced post-resective neurological deficits (100.0%; p = 0.013); of the 10 patients, 3 patients (30.0%) had permanent deficits. On the contrary, of the 5 patients with the ALQ PMC resection, only 1 patient (20.0%) experienced transient motor dysphasia for 3 days after surgery. The neurological risks for the AUQ PMC resection group (n = 10) and the PLQ PMC resection group (n = 8) were 60.0% (6/10) and 62.5% (5/8), respectively. Concerning only permanent neurological impairments, the risk for the PUQ PMC resection was 30.0% (3/10), while that of the other PMC resection was 8.7% (2/23) (Figure 4 and 5).

Neurological outcome after the supplementary motor area resection

Of the 43 patients with SMA resection, 23 patients (53.5%) experienced new, postoperative neurological deficits. Three of these patients experienced permanent deficits (7.0%), and 20 patients (46.5%) experienced transient deficits. (Table 6) Permanent deficits corresponded to contralateral grade 4 motor weakness. Transient deficits included contralateral motor weakness in 16 patients, sensory disturbances in 1 patient, dyspraxia in 1 patient, and motor dysphasia or dysarthria in 6 patients. Three patients experienced both motor weakness and dysphasia, and 1 patient experienced both weakness and

(A)



(B)

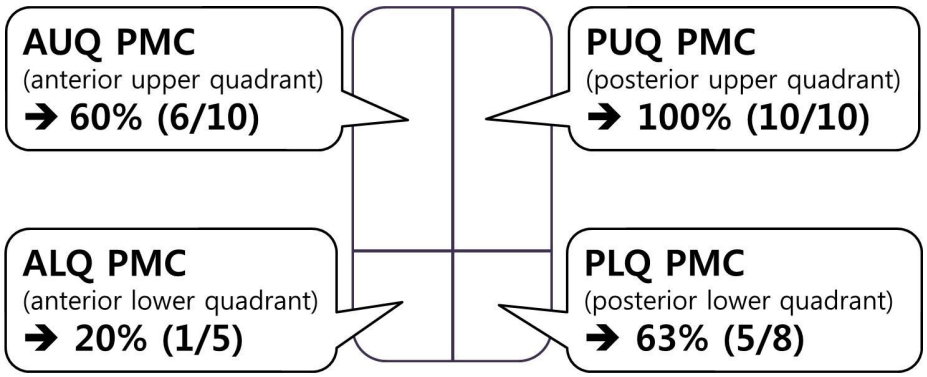


Figure 4

Postoperative neurological risk analysis (A) and schematic diagram (B) according to the topographical resected quadrant area based on the postoperative magnetic resonance image in the 33 patients with the primary motor cortex (PMC) resection (ALQ, anterior lower quadrant; AUQ, anterior upper quadrant; PLQ, posterior lower quadrant; PUQ, posterior upper quadrant)

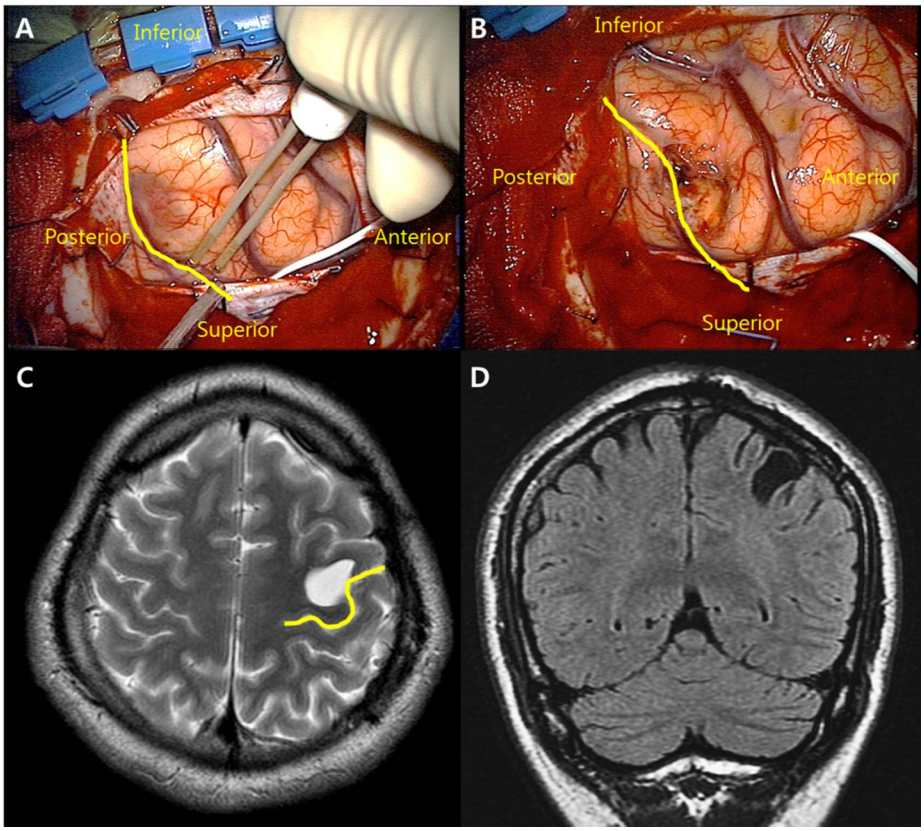


Figure 5

Intraoperative photographs and postoperative brain magnetic resonance images (MRI) of the patient who underwent primary motor cortex resection. The patient (No 29 in Table 3) showed the tumorous lesion in the left precentral gyrus (A) and underwent the lesionectomy and resection of the posterior and middle third precentral gyrus (B). The yellow lines indicate the left precentral sulcus. Postoperative T2-weighted axial (C) and T2-weighted FLAIR coronal (D) MRI depict the resected area. The patient experienced grade 3 right hand weakness for 3 months following surgery.

Table 6

Postoperative neurological risk following the resection of the supplementary motor area (n = 43)

Parameters	Values
Overall neurological deficits	23 (53.5%)
Permanent deficits	3 (7.0%)
Contralateral weakness	3
Transient deficits	20 (46.5%)
Contralateral weakness	15
Dysphasia and speech disturbance	6
Dyspraxia	1
Sensory disturbance	1

dyspraxia. Dyspraxia was characterized by initiation impairment and slowing of skilled and complex movements such as putting on and removing clothing. Of the 20 patients with transient deficits, 13 patients (65%) fully recovered within one month. The mean recovery time was 116 ± 332 days (range, 1 – 1500 days) (Table 7).

In the present study, the SMA was limited posteriorly by the precentral sulcus, inferiorly by the cingulate sulcus, anteriorly by the most rostral point of the genu of the corpus callosum, and laterally by the superior frontal sulcus according to previously described methods. [10, 19, 21] The rostral pre-SMA was defined as the anterior part of the SMA to the vertical line to the anterior commissure (AC) – posterior commissure (PC) plane, crossing the AC (VCA line). The caudal SMA proper was defined as the posterior part of the SMA to the VCA line as per previous reports. [24, 35] (Figure 6)

All 3 patients with permanent hemiparesis underwent resection of the most posterior part of the SMA proper, which is just adjacent to the precentral sulcus. Resection of the most posterior area of the SMA just anterior to the precentral sulcus was performed in 9 patients. Of these 9 patients, 7 (77.8%) experienced postoperative motor weakness. Of the remaining 34 patients, 16 (47.1%) experienced postoperative neurological deficits (p = 0.142). In addition, the risk of developing postoperative neurological deficits was higher in the patients with SMA proper resection (20/32; 62.5%) than in the patients with only pre-SMA resection (3/11; 27.3%; p = 0.078). Resection of both the SMA proper and pre-SMA was associated with postoperative neurological impairments more strongly when compared to resection of either area alone

Table 7

Clinical findings of the 23 patients with postoperative neurological deficits following supplementary motor area resection

No	Sex/ Age	Neurological deficits	Recovery (days)	Resected area	Cingulate gyrus resection
1	F/57	Motor dysphasia	30	SMA proper	Yes
2	M/39	Hand weakness (Gr 4)	270	SMA proper	Yes
3	M/36	Hand weakness (Gr 4)	Permanent	Whole SMA*	Yes
4	M/34	Motor dysphasia, U/E & L/E weakness (Gr 4)	150	Whole SMA	Yes
5	F/15	U/E & L/E weakness (Gr 4)	42	Whole SMA	Yes
6	F/27	U/E weakness (Gr 3)	3	SMA proper	Yes
7	F/43	L/E weakness (Gr 4)	Permanent	SMA proper	No
8	F/43	U/E & L/E weakness (Gr 4)	60	Whole SMA	Yes
9	M/24	U/E & L/E weakness (Gr 4)	14	SMA proper	No
10	M/26	U/E & L/E weakness (Gr 3)	3	Whole SMA	No
11	F/28	Motor dysphasia	30	Pre-SMA	No
12	F/23	U/E & L/E weakness (Gr 4)	5	SMA proper	Yes
13	M/28	Motor dysphasia	30	Whole SMA	No
14	F/17	U/E weakness (Gr 3)	30	Pre-SMA	No
15	M/45	U/E & L/E weakness (Gr 2)	30	Whole SMA	No
16	F/33	U/E & L/E weakness (Gr 4)	Permanent	SMA proper**	No

17	M/40	Motor dysphasia, U/E weakness (Gr 4)	6	SMA proper	Yes
18	M/30	U/E weakness (Gr 3)	60	Whole SMA	No
19	M/40	Hand sensory disturbance	1500	Whole SMA	Yes
20	F/30	U/E & L/E weakness (Gr 4), Motor dyspraxia	8	Whole SMA	Yes
21	M/38	L/E weakness (Gr 4)	42	SMA proper	No
22	M/63	Motor dysphasia, Ankle weakness (Gr 4)	7	SMA proper	No
23	M/30	L/E weakness (Gr 3)	1	Pre-SMA	Yes

* The patient underwent the resection of the most posterior part of the superior, middle, and inferior frontal gyri.

** The patient experienced development of hand weakness during surgery, and the resection stopped.

SMA, supplementary motor area; No, number; F, female; M, male; Gr, grade; U/E, upper extremity; L/E, lower extremity; Whole SMA, whole SMA including SMA proper and pre-SMA

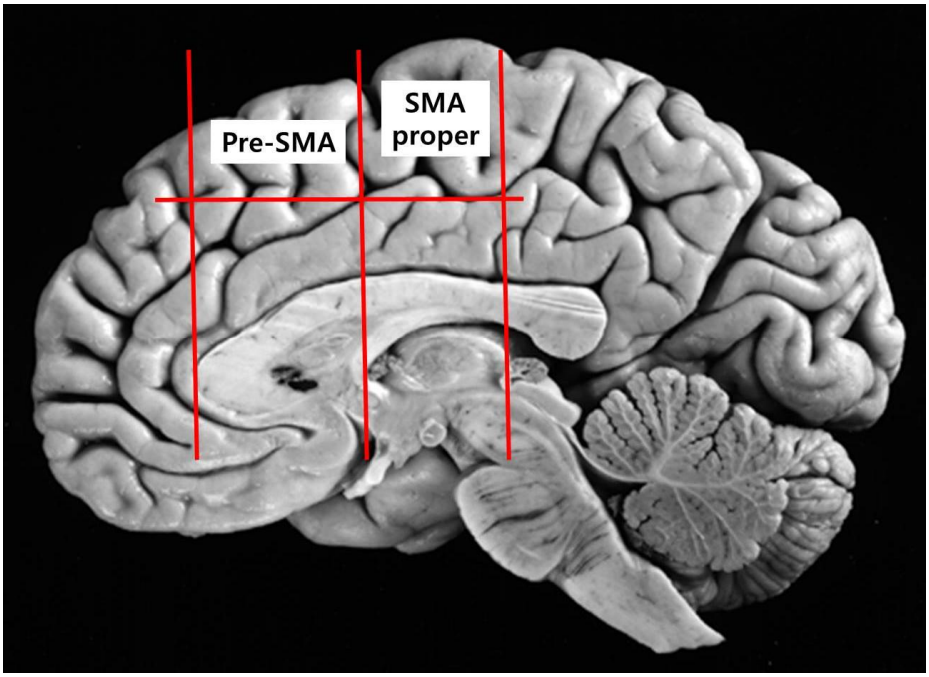


Figure 6

The medial surface of the brain. The rostral pre-supplementary motor area (SMA) was defined as the anterior part of the SMA to the vertical line to the anterior commissure (AC) – posterior commissure (PC) plane, crossing the AC (VCA line). The caudal SMA proper was defined as the posterior part of the SMA to the VCA line. The picture was made by using the image from the website, 'http://163.178.103.176/Temas/Temab2N/APortal/FisoNerCG/LaUII/Neuro/BrainAn/Ch5Text/Section03.html'.

(10/15, 66.7% vs. 13/28, 46.4%; $p = 0.336$).

An analysis of the association between postoperative neurological deficits and resected area, which was stratified by concurrent cingulate gyrus resection, was performed (Figure 7 and 8). Overall, cingulate gyrus resection was significantly related to developing postoperative neurological deficits (12/15; 80.0% vs. 11/28; 39.3%; $p = 0.023$). SMA proper resection with additional cingulate gyrus resection was most strongly related to the development of postoperative neurological deficits when compared to any other type of resection (84.6%; $p = 0.009$). Pre-SMA resection without cingulate gyrus resection was the safest; however, this finding did not reach statistical significance (37.5%; $p = 0.127$). Stratified analysis found that SMA proper resection and additional cingulate gyrus resection was related to postoperative neurological impairments.

Neurological outcome after the primary somatosensory cortex resection

Forty-eight patients underwent the resection of the PSC and/or its adjacent cortex. Based on the removed area of the postoperative MRI, the patients were categorized into 4 groups: group 1 (resection of the PSC only; n = 4), 2 (resection of the PPC only; n = 27), 3 (resection of both PSC and PPC; n = 7), and 4 (resection of both PSC and PMC; n = 10) (Figure 9).

Of the 48 patients, 19 patients (39.6%) experienced new and postoperative neurological deficits. Six of these patients experienced permanent deficits

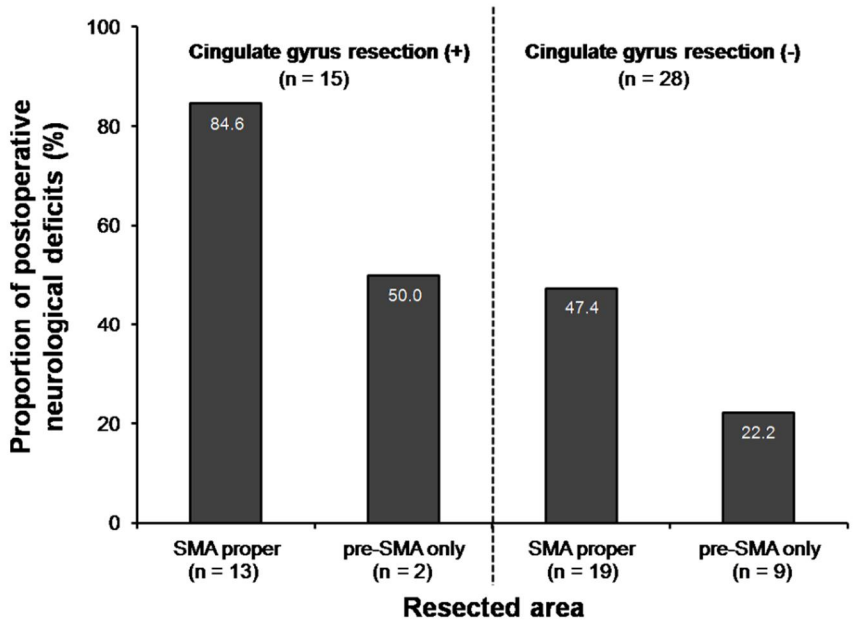


Figure 7

Analysis of the association between the development of new postoperative neurological deficits and the resected area stratified by additional cingulate gyrus resection was performed in patients who underwent supplementary motor area (SMA) resection. Stratified analysis found that cingulate gyrus resection, together with resection of the SMA proper, was associated with postoperative neurological deficits.

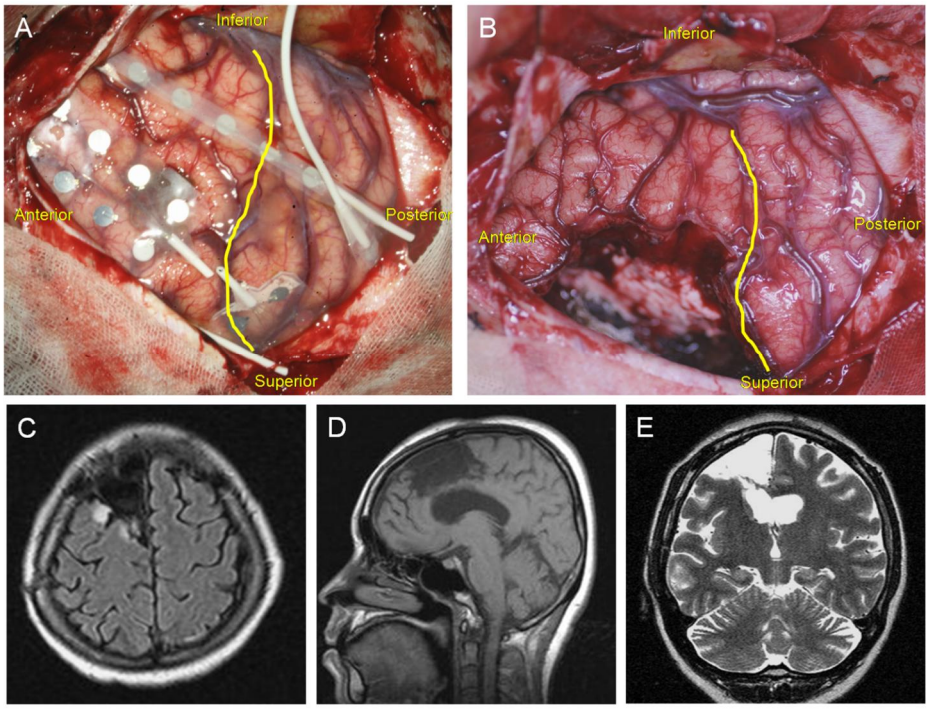
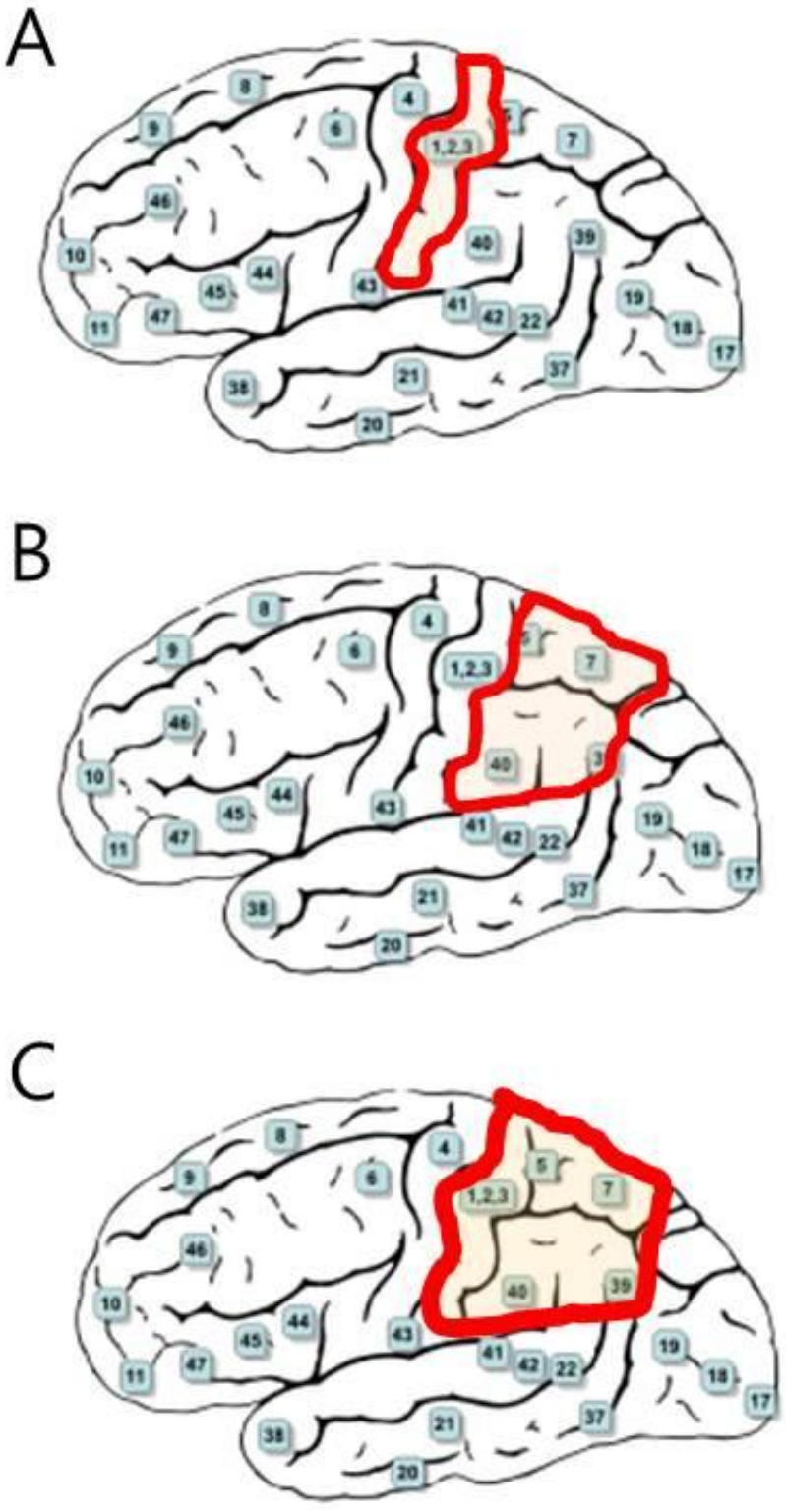


Figure 8

Intraoperative photographs and postoperative brain magnetic resonance images (MRI) of the patient who underwent supplementary motor area resection. The patient underwent subdural grid implantation to localize the ictal onset zone (A) and resection of both the right supplementary motor area and right cingulate gyrus (B). The yellow lines indicate the right precentral sulcus. Postoperative T2-weighted FLAIR axial (C), T1-weighted sagittal (D), and T2-weighted coronal (E) MRI depict the resected area. The patient experienced mild left sided weakness and motor apraxia for 9 days following the surgery.


A
8
4
9
6
1,2,3
7
46
10
40
39
44
45
43
41
42
22
19
18
17
11
47
21
37
38
20
B
8
4
9
6
1,2,3
7
46
40
10
44
45
43
41
42
22
19
18
17
11
47
21
37
38
20
C
8
4
5
9
6
1,2,3
7
46
40
39
10
44
45
43
41
42
22
19
18
17
11
47
21
37
38
20

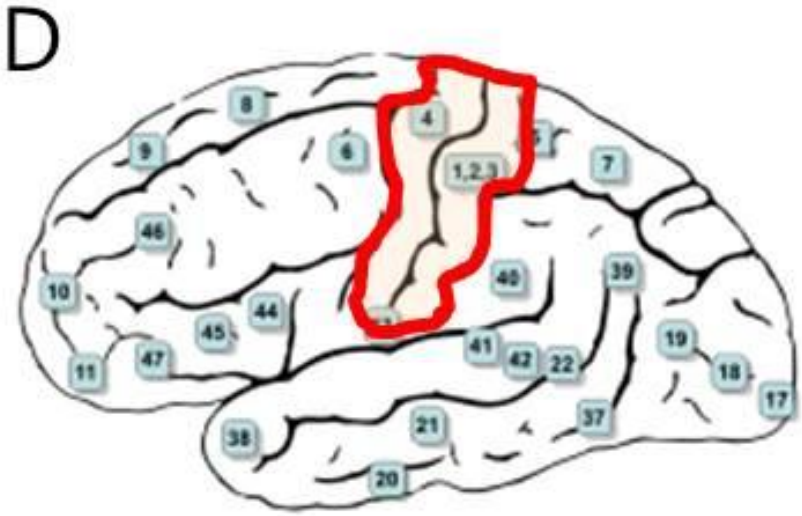


Figure 9

The picture depicts the groups based on the resected area of the patients who underwent the primary somatosensory cortex (PSC): group 1 (resection of the PSC only; A), group 2 (resection of the posterior parietal cortex (PPC) only; B), group 3 (resection of both PSC and PPC; C), and group 4 (resection of both PSC and primary motor cortex; D). The picture was made by using the public domain image (file: Gray726-Brodman.png) from Wikipedia, the free encyclopedia.

(12.5%), and 13 experienced transient deficits (27.1%). (Table 8) The permanent deficits were composed of 3 sensory disturbances, 2 sensory dysphasia and dysarthria, and 1 fine movement disturbance of contralateral hand. The sensory disturbances included 1 hyp- and dysesthesia and 2 equilibrium disorders due to proprioceptive defects. However, the patients who had permanent deficits could live a normal social life because the deficits were not severe. Of the 6 patients, 3 patients were in the group 4 (resection of both PSC and PMC), 2 patients the group 3 (both PSC and PPC), and 1 patient the group 2 (only PPC). Two language disturbances occurred in the patients who underwent the resection of the dominant hemisphere.

Transient deficits included hyp- and dysethesia in 3 patients, proprioceptive deficits in 2 patients, contralateral motor weakness in 3 patients, facial palsy in 1 patient, sensory dysphasia in 2 patients, and Gerstmann syndrome in 2 patients. The sensory dysphasia and Gerstmann syndrome all occurred in the patients who underwent the resection of the dominant hemisphere. Of the 13 patients with transient deficits, 11 patients (84.6%) fully recovered within 3 months. The mean recovery time was 67.5 ± 100.2 days (range, 3 – 300 days). The language-related deficits including 2 permanent sensory dysphasia and dysarthria, 2 transient sensory dysphasia and 2 Gerstmann syndromes were significantly caused by the resection of the dominant hemisphere ($p < 0.001$).

Of the 4 patients of the group 1, only 1 patient (25%) experienced a transient hand hyp- and dysesthesia of contralateral hand. No permanent deficits occurred in the group 1. In the group 2, 4 patients (16.7%) showed postoperative neurological deficits. Three patients who underwent resection of

Table 8

Postoperative neurological risk following the resection of the primary somatosensory cortex and / or its adjacent area (n = 48)

Parameters	Values
Overall neurological deficits	19 (39.6%)
Permanent deficits	6 (12.5%)
Hyp- and dysesthesia	1
Proprioceptive disorder	2
Fine movement disorder	1
Dysphasia or dysarthria	2
Transient deficits	13 (27.1%)
Hyp- and dysesthesia	3
Proprioceptive disorder	2
Contralateral weakness	3
Facial palsy	1
Sensory dysphasia	2
Gerstmann syndrome	2

the Geschwind's territory or its adjacent cortex experienced 2 transient sensory dysphasia and 1 permanent mild dysphasia and dysarthria. The remaining 1 patient who underwent the left parietal lobe resection showed transient acalculia and agraphia, so-called the Gerstmann syndrome.

On the contrary, the neurological risk of the group 3 (Figure 10) reached 80.0% (8/10). Proprioceptive defects causing equilibrium disturbance occurred in 2 patients (20.0%) for a long time, and 6 transient deficits (60.0%) included dysethesia like tingling sensation, disturbance of position sense of hand, proprioceptive deficit, contralateral weakness, facial palsy, and the Gerstmann syndrome. Of the patients, 2 patients suffered from sensory disturbance and the Gerstmann syndrome over 9 months.

In the group 4, 6 patients (60.0%) showed neurological deficits including 3 permanent (30.0%) and 3 transient ones (30.0%). Permanent deficits included hyp- and dysethesia of contralateral hand, mild dysarthria, and fine movement disturbance of hand, and transient deficits included 2 contralateral weaknesses and 1 dysarthria. The neurological risk based on the resection group was summarized in Table 9.

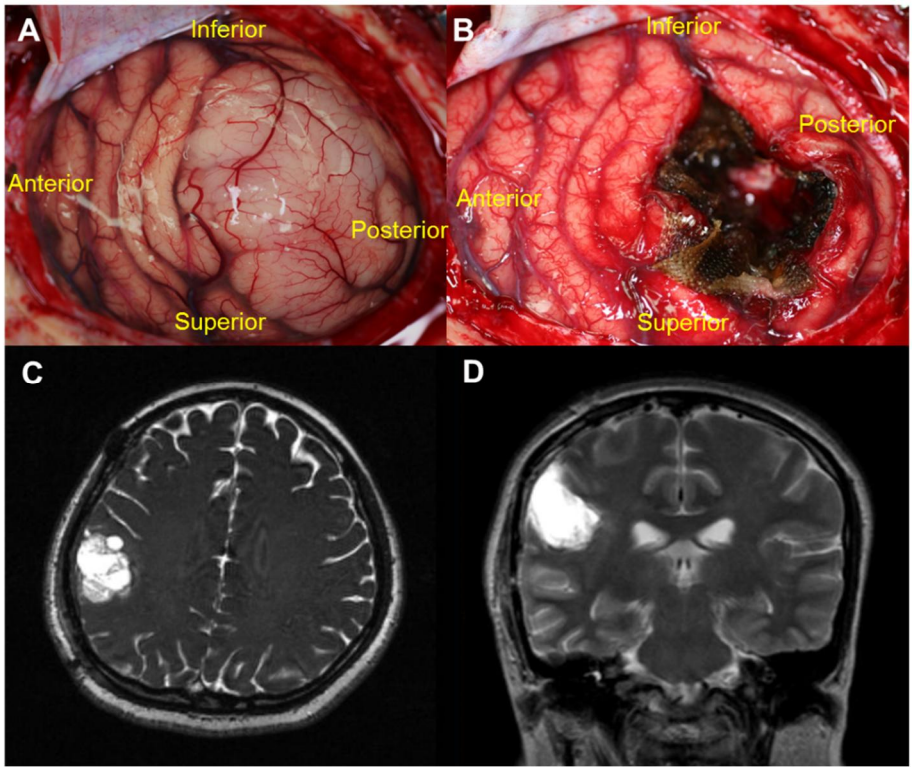


Figure 10

Intraoperative photographs and postoperative brain magnetic resonance images (MRI) of the patient who underwent primary somatosensory cortex resection. The patient showed the whitish tumorous lesion in the posterior part of the right postcentral gyrus and the anterior part of the inferior parietal lobule (A) and underwent the lesionectomy and resection of the both postcentral gyrus and posterior parietal cortex (B). Postoperative T2-weighted axial (C) and coronal (D) MRI depict the resected area. The patient experienced hypesthesia and dysethesia of right arm and face for 9 months after the surgery.

Table 9

Postoperative neurological risk analysis according to the topographical resected area based on the postoperative magnetic resonance image in the 48 patients with the resection of the primary somatosensory cortex (PSC) and / or its adjacent cortices

Resected area	Transient ND	Permanent ND	Total ND
PSC only (n=4)	1 (25.0%)	0 (0.0%)	1 (25.0%)
PPC only (n=24)	3 (12.5%)	1 (4.2%)	4 (16.7%)
PSC and PPC (n=10)	6 (60.0%)	2 (20.0%)	8 (80.0%)
PSC and PMC (n=10)	3 (30.0%)	3 (30.0%)	6 (60.0%)
Total (n=48)	13 (27.1%)	6 (12.5%)	19 (39.6%)

PSC, primary somatosensory cortex; ND, neurological deficits; PPC, posterior parietal cortex; PMC, primary motor cortex

Risk factor analyses

The associations between neurological deficits after PMC resection and several clinico-anatomical factors were evaluated (Table 10). Univariate analysis found that the posterior and upper quadrant PMC resections were related to postoperative neurological deficits; this result was not significant. However, in the multivariate analysis, the posterior quadrant PMC resection (p = 0.022; OR = 14.4; 95% CI, 1.5 – 143.1) and the upper quadrant PMC resection (p = 0.030; OR = 12.4; 95% CI, 1.3 – 120.6) were the only two significant risk factors for postoperative neurological deficits following PMC resection.

Associations between postoperative neurological deficits after SMA resection and several clinico-anatomical factors were evaluated (Table 11). Univariate analysis found that cingulate gyrus resection, shorter lifetime history of seizure (< 10 years), and SMA proper resection (p = 0.023, 0.069, 0.078, respectively) were associated with postoperative neurological impairments after SMA resection. However, cingulate gyrus resection (p = 0.027; OR = 6.5; 95% CI, 1.2 – 34.6) was the only significant risk factor for postoperative neurological deficits identified via multivariate analysis.

The associations between postoperative neurological deficits after the PSC resection and several clinico-anatomical factors were evaluated (Table 12). Univariate analysis found that preoperative neurological deficit (p = 0.036) and both PSC and PPC resection (p = 0.005) were significantly associated with the postoperative new neurological impairments. In the multivariate

Table 10

Risk factors for postoperative neurological deficits following primary motor cortex resection

Factors	Univariate	Multivariate	
	***p* value**	***p* value**	**OR (95% CI)**
Patient sex (male)	1.000	NI	
Patient age (≥ 40 years)	0.721	NI	
Sz duration (< 5 years)	0.703	NI	
Sz frequency (< 2/week)	0.721	NI	
Sz type	0.864	NI	
Preoperative ND	0.246	0.715	
Side of surgery (left side)	0.696	NI	
Type of surgery	0.304	NI	
Intraoperative Sz	1.000	NI	
Posterior quadrant	0.061	**0.022**	**14.4 (1.5 – 143.1)**
Upper quadrant	0.065	**0.030**	**12.4 (1.3 – 120.6)**
PSC resection	0.438	NI	
Operation time (≥ 270min)	0.721	NI	
Histological diagnosis (Tumors)	0.147	0.344	
Unfavorable seizure outcome (Engel's classification III and IV)	0.249	0.378	

OR, odds ratio; CI, confidence interval; Sz, seizure; NI, not included; ND, neurological deficits; PSC, primary somatosensory cortex

Table 11

Risk factors for postoperative neurological deficits following supplementary motor area (SMA) resection

Factors	Univariate	Multivariate	
	***p* value**	***p* value**	**OR (95% CI)**
Patient sex	1.000	NI	
Patient age (>30 years)	**0.131**	0.264	2.3 (0.5 – 9.7)
Sz duration (< 10 years)	**0.069**	0.108	3.4 (0.8 – 15.0)
Sz frequency (<1/week)	0.223	NI	
Sz type	0.758	NI	
Predisposing factor	1.000	NI	
Side of surgery	1.000	NI	
Type of surgery	0.213	NI	
SMA proper resection	**0.078**	0.204	2.9 (0.6 – 14.9)
Pre-SMA resection	0.756	NI	
Both of SMA proper and pre-SMA resection	0.336	NI	
Cingulate gyrus resection	**0.023**	**0.027**	**6.5 (1.2 – 34.6)**
Longer operation time	0.354	NI	
Histological diagnosis (Tumors)	0.206	NI	
Unfavorable seizure Outcome (Engel's classification III and IV)	0.203	NI	

SMA, supplementary motor area; OR, odds ratio; CI, confidence interval; Sz, seizure; Preop, preoperative; NI, not included

Table 12

Risk factors for postoperative neurological deficits following the resection of the primary somatosensory cortex (PSC) and / or its adjacent cortices

Factors	**Univariate**	**Multivariate**	
	***p* value**	***p* value**	**OR (95% CI)**
Patient sex (male)	1.000	NI	
Patient age (≥ 30 years)	0.250	NI	
Sz duration (< 8 years)	0.075	0.070	
Sz frequency (< 3/month)	0.250	NI	
Sz type	0.480	NI	
Predisposing factor	0.853	NI	
Preoperative ND	**0.036**	0.164	
Preoperative MRI findings	0.433	NI	
Side of surgery (left side)	0.387	NI	
Type of surgery	0.691	NI	
Intraoperative Sz	1.000	NI	
Both PSC and PPC resection	**0.005**	**0.002**	**41.8 (4.0 – 433.8)**
Both PSC and PMC resection	0.164	0.057	
Dominant IPL resection	0.438	NI	
Resection volume (< 12cm^3)	0.382	NI	
Operation time (≥ 280min)	1.000	NI	
Histological diagnosis (Tumors)	0.064	0.832	

Unfavorable seizure outcome (Engel's classification III and IV)	0.821	NI

PSC, primary somatosensory cortex; OR, odds ratio; CI, confidence interval; Sz, seizure; NI, not included; ND, neurological deficits; MRI, magnetic resonance imaging; PPC, posterior parietal cortex; PMC, primary motor cortex; IPL, inferior parietal lobule

analysis, the both PSC and PPC resection was the only significant risk factor for postoperative neurological deficit of the S1 area resections ($p = 0.002$; OR = 41.8; 95% CI, 4.0 – 433.8). Overall neurological risk following the MSA resections and the significant topographical risk factors were summarized in the Table 13 and 14.

Table 13

Postoperative overall and permanent neurological risk of the specific factors following the resection of the motor and somatosensory area (n = 109)

Factors	Overall risk		Permanent risk	
	(%)	OR	(%)	OR
Overall neurological risk	47.7		9.2	
Male sex	48.9		11.3	
Age (> 40 years)	58.3		12.5	
Sz duration (< 6 years)	54.2		10.4	
Sz frequency (< 1/week)	52.5		10.2	
No predisposing factors	50.0		10.3	
Preoperative ND	**76.0**	**4.89***	**20.0**	**3.95***
No preresective invasive study	**61.1**	**2.81***	11.1	
Dominant hemisphere	49.2		**13.8**	**6.91***
Primary motor cortex	**63.6**	**2.54***	15.2	
Supplementary motor area	53.5		7.0	
Primary somatosensory cortex	62.5		12.8	
Additional resection of the adjacent areas	**68.1**	**4.48***	**14.9**	**3.44***
Larger resection volume	39.3		10.7	
Longer operation time (> 5hrs)	52.3		9.1	
Tumorous lesions	**63.0**	**2.97***	8.7	
Unfavorable seizure outcome (Engel's classification III - IV)	60.6		18.2	

* The *p* value was < 0.05. OR; odds ratio, Sz; seizure, ND; neurological deficit

Table 14

Overall neurological risk following the motor and somatosensory resections and the significant topographical risk factors

Parameters	Values
Overall neurological risk (n =109)	
Overall risk	47.7%
Transient ND risk	38.5%
Permanent ND risk	9.2%
Primary motor area (n = 33)	
Overall risk	66.7%
Transient ND risk	51.5%
Permanent ND risk	15.2%
Risk factor	Posterior and upper area of the primary motor cortex
Supplementary motor area (n = 43)	
Overall risk	53.5%
Transient ND risk	46.5%
Permanent ND risk	7.0%
Risk factor	Additional resection of the cingulate gyrus
Primary somatosensory area (n = 48)	
Overall risk	39.6%
Transient ND risk	27.1%
Permanent ND risk	12.5%
Risk factor	Additional resection of the posterior parietal cortex

ND; neurological deficit

DISCUSSION

Since resective surgery with intraoperative mapping and neurological monitoring under awake anaesthesia was developed, eloquent cortical resections, including MSA resections, are no longer impossible procedures.[11, 12] Many previous reports, however, could not demonstrate why some patients suffered from postoperative neurological sequelae, while others did not following resection and did not propose the way how neurosurgeons could avoid the postoperative neurological complications of MSA resections. The author focused on the implication of the adjacent non-eloquent area and hypothesized that the additional resection of the adjacent area of the MSA could increase the postoperative neurological risk.

In terms of the PMC resection, the additional resection of the adjacent area (e.g., SMA or PSC) showed the tendency of higher neurological risk, but not the significance. The specific location of the resected area in the PMC was more important risk factor rather than the additional resection. In case of the SMA and PSC resections, however, the additional resection of the cingulate gyrus and PPC was the most significant risk factors for the new postoperative neurological deficits, respectively.

Primary motor cortex resection

Resection of the posterior part of the PMC was the most notable risk factor

for developing postoperative neurological impairments following PMC resection. To our knowledge, no study has focused on the relationship between the anterior-posterior location of the PMC resection and the neurological outcome. The present study provided limited but significant evidence that the posterior portion of the PMC is more vulnerable to post-resective neurological morbidities than the anterior part. The evidence of this phenomenon can be found in any traditional guide to cortical anatomy, including a Brodmann map.[17] Of the Brodmann areas, the Brodmann area 4 is located in the posterior part of the PMC. In particular, the width of Brodmann area 4 is wider at the upper third of the PMC and narrower at the lower third, and the shape of area 4 is an inverted triangle (Figure 11).[17] In other words, the core of primary motor function may be located in the posterior part of the PMC, whereas the anterior part of the PMC, especially, the lower third of the gyrus may be relatively less functional area, and thus, may be more resistant to possible post-resective neurological deficits. The present data demonstrate clinical evidence for the topographical validity of Brodmann's area 4.

In addition, the lower third part of the PMC was the safest area in terms of post-resective neurological morbidities (compared to the upper two thirds) in this study. As mentioned above, the width of Brodmann area 4 gradually gets narrower at more posterior parts towards the inferior end of the PG. This inverted triangle shape of area 4 coincides with the results of this study. Of the 4 quadrants of the PMC, the anterior and lower part was the safest for resection and the posterior and upper part was the most vulnerable area, which can be explained by the shape and location of Brodmann area 4. The fact that

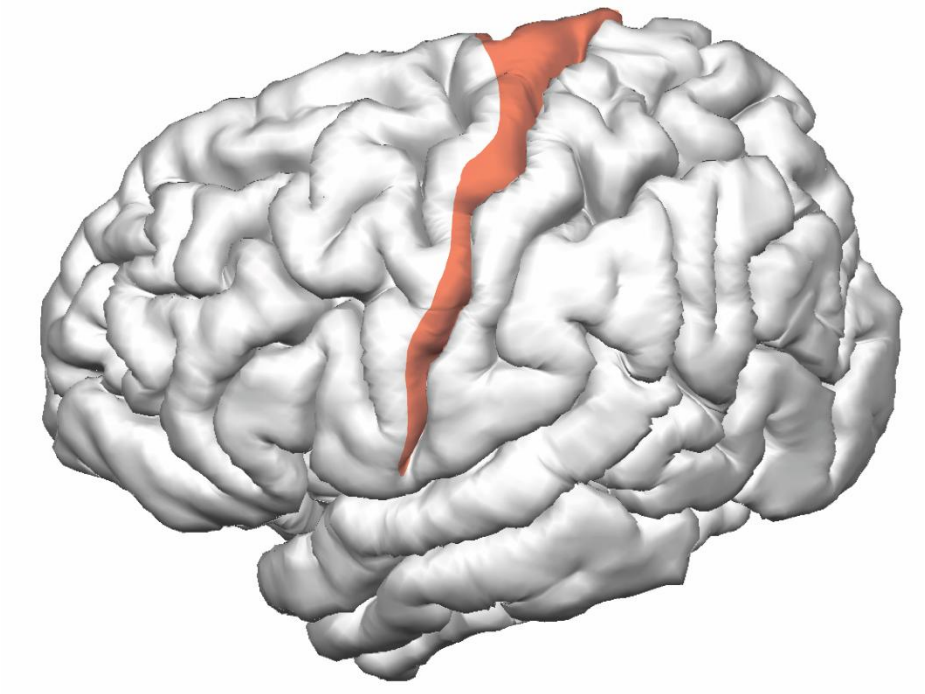


Figure 11

The picture depicts the Brodmann area 4 on the precentral gyrus. The width of Brodmann area 4 gradually becomes narrower toward the lower end of the precentral gyrus, and this area is located at the posterior part of the precentral gyrus along the central sulcus.

unilateral excision of the lower part of the PMC, which corresponds to the face and tongue motor area, was not associated with significant long-term neurological sequelae has previously been well-known.[11, 16] This may be due to the bilateral cortical representation of the face and tongue area.[11, 16] This bilateral cortical projection may cause the lower post-resective neurological risk of the lower third of the PMC.

Supplementary motor area resection

Not all patients who undergo SMA resection experience postoperative neurological impairments such as SMA syndrome. Initial reports found that the SMA syndrome occurred in every SMA resection patient. [15, 25] However, the overall incidence rate of SMA syndrome is variable, ranging from 23% to 100% according to recent series. [9, 10, 24, 27] In the present study, only 53.5% of patients experienced postoperative neurological deficits. In other words, while some patients who undergo SMA resection recover well without any neurological complications, other patients with the same procedure experience motor weakness or language problems lasting as long as several months. Moreover, these neurological conditions greatly impact patients' quality of life. Therefore, it is essential to explore the risk factors associated with neurological deficits that follow SMA resection. Controlling these risk factors before and during surgical resection may lead to improved clinical care.

Resection of the cingulate gyrus was the most notable risk factor for developing postoperative neurological impairments following SMA resection.

The cingulate gyrus is a major medial cortical structure that overlies the corpus callosum from the lamina terminalis rostrally to the splenium at its caudal extent. [20, 29] Traditionally, the cingulate gyrus has been associated with limbic and emotion pathways. [33] However, recent neurophysiologic and neuroanatomical studies of humans and animals have dramatically changed the understanding of cingulate function. [20] Specifically, the cingulate cortex has been recognized to consist of 4 divisions, each with a unique function: the perigenual anterior cingulate cortex (pACC), the midcingulate cortex (MCC), the posterior cingulate cortex (PCC), and the retrosplenial cortex (RSC). [33] Among these cortices, the MCC comprises approximately one-third of the total cingulate cortex beneath the SMA, and it functions to 1) select an appropriate motor response based on its motivational significance and 2) carry out that response via direct connections to the spinal cord, limbic cortices, and primary or supplementary motor areas. [18, 29] The other cortices, the pACC, PCC, and RSC, are associated with emotional, visuospatial, or memory functions rather than motor functions. [4, 29, 30, 33] Resected cingulate cortical areas corresponded to the MCC beneath the SMA in this study. Moreover, the 12 patients who underwent resection of both the SMA and cingulate gyrus experienced postoperative motor weakness or apraxia. The resected area of the cingulate gyrus may thus be responsible for motor functions because resecting this area produces motor impairments.

In our opinion, cingulate gyrus resection has not been studied adequately. Tate et al. [29] reported on 90 resections of cingulate gyrus gliomas, the largest surgical series to date. In their study, a high rate of postoperative morbidity,

such as SMA syndrome, was induced by resection of the MCC or PCC when compared to resection of the pACC. The authors demonstrated that these morbidities occurred only in cases with SMA resection as a surgical trajectory. Therefore, postoperative neurological impairments associated with cingulate cortical resection may be induced by SMA damage. This phenomenon was also found in a recent series reported by von Lehe et al. [34] In their 22 resective surgeries for cingulate gyrus epilepsy, extra-cingulate resection including the SMA induced SMA syndrome. The previous 2 studies [29, 34] and the present study report that resection of both the SMA and cingulate gyrus induces postoperative neurological deficits. Consequently, SMA resection, when accompanied by resection of the cingulate cortex below it, is prone to cause postoperative neurological deficits, although, the exact mechanism of this and the connections between these 2 areas require further study.

Primary somatosensory cortex resection

The postoperative neurological risk of the resection of the PSC only was just 25%, though only 4 patients underwent the resection of the postcentral gyrus only. Only 1 patient experienced transient contralateral hand hypesthesia and mild facial palsy; this patient had a full recovery. A number of previous authors have reported an acceptable outcome after the PSC resection.[1, 5, 6, 14, 23] The favourable outcome of the PSC resection may result from the enhanced cortical plasticity and function reorganization present in epilepsy patients.[14]

However, the overall postoperative neurological risk in this study was not

low (39.6%), and the risk of the whole patients who underwent the resection of the PSC reached 62.5% (15/24). The postoperative neurological deterioration following PSC resection might be underestimated in the literature, because the neurological evaluation after the PSC resection could be ambiguous. The most frequent deficits following PSC resection, including sensory disturbances, could be subjective and not easy to be assessed. To our knowledge, no objective assessment protocol or grade was proposed to evaluate the sensory function disorder. Therefore, these vague symptoms could be missed during intraoperative neurological monitoring. In this study, it is also the most difficult to detect the patients' sensory deficits such as hypesthesia, dysethesia, or proprioceptive defects, especially when the symptoms were mild and transient during the follow-up periods. Some patient, however, who suffered from the proprioceptive disorders of his or her lower extremities, complained of equilibrium disorders or even gait disturbance. Others experienced language disorders such as sensory dysphasia may be due to the resection the Geschwind's territory or its adjacent cortex, which was located at rather PPC than PSC.

The resection of the PPC in addition to PSC resection was the most notable risk factor for developing postoperative neurological impairments in this study. The PPC has been known to play an important role in planned movements, spatial reasoning, and attention. The PPC receives neuro-physiological inputs from the three sensory systems, including visual, auditory, and somatosensory systems and sends outputs to the frontal motor areas.[26, 31, 32] Although the neurological results after the PPC resection in a large series has not been

reported, damage of the PPC can develop a variety of sensorimotor deficits, including deficits in the perception, accurate reaching and grasping, and the control of eye movement. In this study the postoperative neurological risk of the PPC resection was not high (16.7%), while that of the both PSC and PPC resection was significant high (80.0%). Unfortunately, the exact mechanism of the discrepancy of the neurological risk cannot be proven, however, the disruption of the connection between the PSC and PPC might cause worse neurological prognosis. The damage of the both PSC and PPC might block the neuro-physiological information not only from the PSC, but also from the visual and auditory systems. Especially, the disruption of transmission from the somatosensory and visual systems to frontal motor areas could cause neurological deficits such as equilibrium disorder and gait disturbance without lower limb weakness. Moreover, the injury of the compensatory area, which might be the PPC near the PSC in this study, could interfere with cortical plasticity and functional reorganization and result in the worse neurological outcome.

Another notable finding of this study was that the neurological risk of the both PSC and PPC resection was higher than even that of the both PSC and PMC resection. The damage of the PMC can easily develop the neurological sequelae such as contralateral weakness or facial palsy. However, the intraoperative cortical stimulation and neurological monitoring under awake anesthesia could reduce the postoperative deficits including contralateral weakness and language function.[11-13] On the contrary, the sensory disturbances following injury of the PSC were possible to be under-estimated during

intraoperative monitoring.

Significances of the additional resection of the adjacent areas

The author hypothesized that the additional resection of the adjacent area of the MSA could increase the postoperative neurological risk. The results of the present study proved the hypothesis to a certain degree. The additional resection of the PPC and cingulate gyrus significantly increased the postoperative neurological risk of the resection of the PSC and SMA. Therefore, the postoperative neurological outcomes and deficits may be influenced by not the damage of the only eloquent center (e.g. PSC and SMA), but the disruption of the neurophysiological connections between the eloquent area and its adjacent non-eloquent areas or the total amount of damage of both these two areas. The findings imply that the eloquent center of the motor and somatosensory functions work not by alone, but by integration or cooperation with the adjacent non-eloquent areas.

However, the additional resection of the SMA, PSC, or premotor frontal areas could not increase the postoperative neurological risk significantly. This result may be caused by the difference of the functional unit of the PMC as a final executional organ compared with the PSC or SMA. The additional significance of the premotor frontal area should be examined.

Limitations

The inclusion of heterogeneous disease groups and the retrospective nature of the study may have affected the results directly or indirectly. In addition, the present study considered only the cortical resected area but did not take into account the depth of the resection reaching the underlying white matter. Actually, the language disturbances including dysphasia and dysarthria may not be caused by the damage of the Broca's or Wernicke's area, but of the deeper white matter structures such as arcuate fasciculus or superior longitudinal fasciculus. In addition, the tendency of the higher neurological risk of the patients with tumorous lesions could result from the damage of the peri-tumoral white matter rather than that of the cortical areas. The last limitation was absence of the objective assessment tool for the sensory impairments. This limitation could result in the uncertainty of the postoperative neurological status after the PSC resection.

CONCLUSION

After the resection of the MSA and its adjacent area, 48% of the patients experienced neurological impairments including 9% of the permanent deficits. The PUQ of the PMC were more vulnerable to post-resective neurological deficits than the ALQ. The additional resection of the cingulate gyrus and the PPC increased significantly the postoperative neurological risk after the SMA and PSC resection, respectively. The results imply that the postoperative neurological outcomes and deficits were influenced by not the damage of the only eloquent center, but the disruption of the neurophysiological connections between the eloquent area and its adjacent non-eloquent areas or the total amount of damage of both these two areas. Taking these risk factors into account before and during surgical resection may lead to improved clinical care.

REFERENCES

1. Asano E, Ishikawa S, Otsuki T, Nakasato N, Yoshimoto T: Surgical treatment of intractable epilepsy originating from the primary sensory area of the hand--case report. **Neurologia medico-chirurgica** 39: 246-250, 1999.
2. Benifla M, Sala F, Jr., Jane J, Otsubo H, Ochi A, Drake J, et al.: Neurosurgical management of intractable rolandic epilepsy in children: role of resection in eloquent cortex. Clinical article. **J Neurosurg Pediatr** 4: 199-216, 2009.
3. Berger MS, Kincaid J, Ojemann GA, Lettich E: Brain mapping techniques to maximize resection, safety, and seizure control in children with brain tumors. **Neurosurgery** 25: 786-792, 1989.
4. Chassagnon S, Minotti L, Kremer S, Hoffmann D, Kahane P: Somatosensory, motor, and reaching/grasping responses to direct electrical stimulation of the human cingulate motor areas. **J Neurosurg** 109: 593-604, 2008.
5. Cohen-Gadol AA, Britton JW, Collignon FP, Bates LM, Cascino GD, Meyer FB: Nonlesional central lobule seizures: use of awake cortical mapping and subdural grid monitoring for resection of seizure focus. **J Neurosurg** 98: 1255-1262, 2003.
6. Cohen-Gadol AA, Ozduman K, Bronen RA, Kim JH, Spencer DD: Long-term outcome after epilepsy surgery for focal cortical dysplasia. **J Neurosurg** 101: 55-65, 2004.

7. de Oliveira RS, Santos MV, Terra VC, Sakamoto AC, Machado HR: Tailored resections for intractable rolandic cortex epilepsy in children: a single-center experience with 48 consecutive cases. **Childs Nerv Syst** 27: 779-785, 2011.

8. Engel J, Van Ness PC, Rasmussen TB: Outcome with respect to epileptic seizures. In: Engel J, ed.: *Surgical treatment of the epilepsies 2nd Ed.* New York: Raven Press, 1993, pp609-621.

9. Fontaine D, Capelle L, Duffau H: Somatotopy of the supplementary motor area: evidence from correlation of the extent of surgical resection with the clinical patterns of deficit. **Neurosurgery** 50: 297-303; discussion 303-295, 2002.

10. Kasasbeh AS, Yarbrough CK, Limbrick DD, Steger-May K, Leach JL, Mangano FT, et al.: Characterization of the supplementary motor area syndrome and seizure outcome after medial frontal lobe resections in pediatric epilepsy surgery. **Neurosurgery** 70: 1152-1168, 2012.

11. Kim YH, Kim CH, Kim JS, Lee SK, Chung CK: Resection frequency map after awake resective surgery for non-lesional neocortical epilepsy involving eloquent areas. **Acta Neurochir (Wien)** 153: 1739-1749, 2011.

12. Kim YH, Kim CH, Kim JS, Lee SK, Han JH, Kim CY, et al.: Risk factor analysis of the development of new neurological deficits following supplementary motor area resection. **J Neurosurg** 119: 7-14, 2013.

13. Kim YH, Kim CH, Kim JS, Lee SK, Han JH, Kim CY, et al.:

Topographical Risk Factor Analysis of New Neurological Deficits Following Precentral Gyrus Resection. **Neurosurgery**, 2015.

14. Koubeissi MZ, Maciunas RJ, Tanner A, Luders HO: Medically intractable seizures originating from the primary somatosensory hand area. **Epileptic disorders : international epilepsy journal with videotape** 10: 339-348, 2008.

15. Laplane D, Talairach J, Meininger V, Bancaud J, Orgogozo JM: Clinical consequences of corticectomies involving the supplementary motor area in man. **J Neurol Sci** 34: 301-314, 1977.

16. Lehman R, Andermann F, Olivier A, Tandon PN, Quesney LF, Rasmussen TB: Seizures with onset in the sensorimotor face area: clinical patterns and results of surgical treatment in 20 patients. **Epilepsia** 35: 1117-1124, 1994.

17. Loukas M, Pennell C, Groat C, Tubbs RS, Cohen-Gadol AA: Korbinian Brodmann (1868-1918) and his contributions to mapping the cerebral cortex. **Neurosurgery** 68: 6-11; discussion 11, 2011.

18. Morecraft RJ, Van Hoesen GW: Cingulate input to the primary and supplementary motor cortices in the rhesus monkey: evidence for somatotopy in areas 24c and 23c. **J Comp Neurol** 322: 471-489, 1992.

19. Nelson L, Lapsiwala S, Haughton VM, Noyes J, Sadrzadeh AH, Moritz CH, et al.: Preoperative mapping of the supplementary motor area in patients harboring tumors in the medial frontal lobe. **J Neurosurg** 97: 1108-1114, 2002.

20. Paxinos G, Mai JK: *The Human Nervous System, ed. 2.* Amsterdam: Elsevier Academic Press, 2004.

21. Penfield W, Welch K: The supplementary motor area of the cerebral cortex; a clinical and experimental study. **AMA Arch Neurol Psychiatry** 66: 289-317, 1951.

22. Pilcher C, Meacham WF, Holbrook TJ: Partial excision of the motor cortex in treatment of jacksonian convulsions; results in 41 cases. **Archives of surgery** 54: 633-643, 1947.

23. Pondal-Sordo M, Diosy D, Tellez-Zenteno JF, Girvin JP, Wiebe S: Epilepsy surgery involving the sensory-motor cortex. **Brain** 129: 3307-3314, 2006.

24. Rosenberg K, Nossek E, Liebling R, Fried I, Shapira-Lichter I, Hendler T, et al.: Prediction of neurological deficits and recovery after surgery in the supplementary motor area: a prospective study in 26 patients. **J Neurosurg** 113: 1152-1163, 2010.

25. Rostomily RC, Berger MS, Ojemann GA, Lettich E: Postoperative deficits and functional recovery following removal of tumors involving the dominant hemisphere supplementary motor area. **J Neurosurg** 75: 62-68, 1991.

26. Rushworth MF, Behrens TE, Johansen-Berg H: Connection patterns distinguish 3 regions of human parietal cortex. **Cereb Cortex** 16: 1418-1430, 2006.

27. Russell SM, Kelly PJ: Incidence and clinical evolution of postoperative deficits after volumetric stereotactic resection of glial

neoplasms involving the supplementary motor area. **Neurosurgery** 52: 506-516; discussiom 515-506, 2003.

28. Shinoura N, Yoshida M, Yamada R, Tabei Y, Saito K, Suzuki Y, et al.: Awake surgery with continuous motor testing for resection of brain tumors in the primary motor area. **J Clin Neurosci** 16: 188-194, 2009.

29. Tate MC, Kim CY, Chang EF, Polley MY, Berger MS: Assessment of morbidity following resection of cingulate gyrus gliomas. Clinical article. **J Neurosurg** 114: 640-647, 2011.

30. Turken AU, Swick D: Response selection in the human anterior cingulate cortex. **Nat Neurosci** 2: 920-924, 1999.

31. Valyear KF, Frey SH: Human posterior parietal cortex mediates hand-specific planning. **Neuroimage**, 2015.

32. Vingerhoets G: Contribution of the posterior parietal cortex in reaching, grasping, and using objects and tools. **Front Psychol** 5: 151, 2014.

33. Vogt BA: Pain and emotion interactions in subregions of the cingulate gyrus. **Nat Rev Neurosci** 6: 533-544, 2005.

34. von Lehe M, Wagner J, Wellmer J, Clusmann H, Kral T: Epilepsy surgery of the cingulate gyrus and the frontomesial cortex. **Neurosurgery** 70: 900-910, 2012.

35. Zilles K, Schlaug G, Matelli M, Luppino G, Schleicher A, Qu M, et al.: Mapping of human and macaque sensorimotor areas by integrating architectonic, transmitter receptor, MRI and PET data. **J Anat** 187 (Pt 3): 515-537, 1995.

국문 초록

서론: 운동 및 감각 뇌기능 영역 제거 수술은 수술 후에 신경학적 결손이 심하기 때문에 쉽지 않다. 저자는 운동 및 감각 뇌기능 영역 제거 수술 시에 비기능 주변 영역을 추가 절제한 경우 신경학적 예후가 좋지 않을 것이라고 가설을 세웠다. 본 연구에서는 운동 및 감각 영역 제거를 시행한 후의 신경학적 결손 정도를 조사하고, 이에 미치는 국소 해부학적인 예후 인자를 알아보고자 하였다.

대상 및 방법: 본 연구에서는 운동 및 감각 영역과 더불어 비기능 주변 영역을 각성 시 뇌수술로 제거한 환자들 109 명의 영상 자료와 임상 자료를 분석하였다. 이 중에서 33 명의 일차 운동 피질 (primary motor cortex) 을 제거한 환자, 43 명의 보조 운동 영역 (supplementary motor area) 을 제거한 환자, 24 명의 일차 감각 피질 (primary sensory cortex) 을 제거한 환자를 선정하였다. 제거 부위에 대한 국소 해부학적인 분석은 수술 전, 후 MRI 영상을 바탕으로 시행되었다.

결과: 일차 운동 피질을 제거한 경우 67% 의 환자들이 수술 후 신경학적 결손을 보였고, 이 중에서 15% 는 영구적인 결손이었다. 주변 영역의 추가 절제 여부는 신경학적 악화와 상관 관계가 없었고, 일차 운동 피질의 뒤쪽, 위쪽 부분을 제거한 경우에 신경학적 악화와 유의한 관련이 있었다. 보조 운동 영역을 제거한 경우 총 47% 환자들이 신경학적 악화 소견을 보였고, 이는 추가로 대상회 (cingulate gyrus) 를 제거한 것과 유의한 상관 관계를 보였다. 일차 감각 피질을 제거한 경우 40% 의 환자들이 수술 후 신경학적

결손을 보였다. 일차 감각 피질에 더해 후 두정엽 피질 (posterior parietal cortex) 을 추가로 제거한 경우 신경학적 위험성이 유의하게 증가하였다.

결론: 운동 및 감각 뇌 영역을 절제한 경우 48% 환자들이 수술 후 신경학적 악화를 경험하였고, 이 중에서 9% 는 영구적이었다. 운동 및 감각 뇌 영역 이외에 추가로 대상회나 후 두정엽 피질을 제거한 경우 수술 후 신경학적 악화는 유의하게 증가하였다. 이러한 결과는 운동 및 감각 영역 제거 후 발생하는 신경학적 결손은 주요 기능 부위만의 제거나 손상 보다는 주요 기능과 그 주변 영역의 통합적인 손상이나 그 두 부위의 전기 신호적 연결 망의 손상에서 기인한다고 볼 수 있다.

주요어 : 일차 운동 피질, 일차 감각 피질, 보조 운동 영역, 대상회, 후 두정엽 피질

학 번 : 2011 – 30592