

Intraoperative Motor Symptoms during Brain Tumor Resection in the Supplementary Motor Area (SMA) without Positive Mapping during Awake Surgery

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Abstract

Awake surgery could be a useful modality for lesions locating in close proximity to the eloquent areas including primary motor cortex and pyramidal tract. In case with supplementary motor area (SMA) lesion, we often encounter with intraoperative motor symptoms during awake surgery even in area without positive mapping. Although the usual recovery of the SMA syndrome has been well documented, rare cases with permanent deficits could be encountered in the clinical setting. It has been difficult to evaluate during surgery whether the intraoperative motor symptoms lead to postoperative permanent deficits. The purpose of this study was to demonstrate the intraoperative motor symptoms could be reversible, further to provide useful information for making decision to continue surgical procedure of tumor resection. Eight consecutive patients (from July 2012 to June 2014, six men and two women, aged 33–63 years) with neoplastic lesions around the SMA underwent an awake surgery. Using a retrospective analysis of intraoperative video records, intraoperative motor symptoms during tumor resection were investigated. In continuous functional monitoring during resection of SMA tumor under awake conditions, the following motor symptoms were observed during resection of the region without positive mapping: delayed motor weakness, delay of movement initiation, slowness of movement, difficulty in dual task response, and coordination disturbance. In seven patients hemiparesis observed immediately after surgery recovered to preoperative level within 6 weeks. During awake surgery for SMA tumors, the above-mentioned motor symptoms could occur in area without positive mapping and might be predictors for reversible SMA syndrome.

Key words: awake surgery, glioma, motor symptom, supplementary motor area

Introduction

In the eloquent area, which includes the supplementary motor area (SMA), the usefulness of a craniotomy under awake conditions has been reported.^{1–4} Positive motor responses, including hypertonia or acceleration of voluntary movement, and negative motor responses, including inhibition of the initiation and continuance of voluntary movements, were observed by cortical and subcortical direct electrical stimulation (DES). These positive mapping areas were often identified as unresectable eloquent areas.^{5–7} DES of the SMA and subcortical frontal lobe generally induced negative motor responses,^{6,8}

which resulted in residual tumor tissues. In addition, without negative motor responses (without positive mapping) by DES, particular motor symptoms including movement disturbance are often encountered during awake surgery in case with SMA lesion. Immediately following surgical resection of the SMA, symptoms known as SMA syndrome including global akinesia, which is worse contralaterally, or speech arrest develop,⁹ and its incidence was reported as approximately 30% to 90%.^{10–12} Though the severity of the movement disturbance varies according to the degree of the SMA resection, near complete recovery of the disturbances can be expected.^{3,12} While surgeons encounter with particular motor symptoms without positive mapping by DES during awake surgery, it should be difficult to evaluate

Received September 28, 2014; Accepted December 19, 2014

whether the motor symptoms lead to postoperative permanent deficits or transient morbidities as SMA syndrome described above.

The SMA is considered as a center for the higher control for voluntary movements; it plays a role in bilateral hand movements and self-pace of consecutive movements.^{13–15} Moreover, the SMA activates during the preliminary stage of a movement and controls the time until movement initiation.¹⁶ Therefore, in an awake surgery of the SMA, various disorders of coordination movements may be induced. However, to our knowledge, no study has provided a detailed report of the motor symptoms during awake surgeries of the SMA.

The usefulness of awake surgery for SMA lesions is still debatable because the usual recovery of the postoperative SMA syndrome can lead to unnecessary intraoperative mapping. Nonetheless, the mechanism of recovery is unclear, and the possibility of permanent morbidities cannot be ruled out in any of the cases. Thus, increasing the documented experiences of intraoperative mapping during SMA tumor resection and delineating its role in overall management is important for safe surgeries.

In this study, we report for the first time that the intraoperative motor symptoms during SMA resection without positive mapping area could be reversible.

Methods

I. Patients

A consecutive series of eight right-handed patients (six men and two women, aged 33–63 years) with glioma located in the SMA region, who underwent an awake surgery in Kanazawa University Hospital between July 2012 and June 2014, were studied. Patients' intraoperative video

records were analyzed for retrospective study. In preoperative neuropsychological examinations, some patients had disorders of attention (Patients 1, 2, 3, 5, 6, and 8), processing speed (Patients 3 and 5), and visuospatial cognition (Patient 8), but this did not have an influence on the intraoperative tasks. Language functions were evaluated preoperatively with the Western Aphasia Battery, and no defects in language function were observed in any patient. Detailed patient information is shown in Table 1. This study was performed according to the guidelines of the Institutional Review Board of the Kanazawa University Hospital. Written informed consents for the use of the patient's images and surgical procedures were obtained from all the patients.

II. Preoperative motor function

The severity of motor weakness was evaluated using Brunnstrom's recovery stage (BRS).¹⁷ The recovery stages are as follows: Stage I—flaccidity of the involved limb is present and no movement can be observed; Stage II—minimal voluntary movement responses are present and spasticity begins to develop; Stage III—basic limb synergies and spasticity become the most severe, and patients find it hard to control voluntary movement; Stage IV—spasticity begins to decline but the influence of spasticity on non-synergistic movement is still observable; Stage V—although mild spasticity is present, more difficult movement combinations are mastered as the limb synergies are lost; and Stage VI—since spasticity disappears, individual joint movements and coordination movements approach normalcy.

Mild paralysis was found in the right hand with Patient 3 (BRS VI), the left leg with Patient 4 (BRS V), and the left hand and fingers with Patient 7 (BRS V

Table 1 Patient characteristics

Patient	Age, sex	Handedness	Tumor location	Diagnosis	WHO grade
1	33, F	R	L sole SMA	Diffuse astrocytoma	II
2	44, M	R	L sole SMA	Diffuse astrocytoma	II
3	43, M	R	L SFG incl. SMA, CG	Anaplastic astrocytoma	III
4	38, M	R	R SFG incl. SMA	Oligodendroglioma	II
5	61, M	R	R SFG incl. SMA, MFG, M, I	Oligodendroglioma	II
6	57, M	R	R SFG incl. SMA, M	Diffuse astrocytoma	II
7	44, M	R	R SFG incl. SMA, MFG, M, CG, CC	Glioblastoma	IV
8	63, F	R	R SFG incl. SMA, MFG, CG, CC	Oligodendroglioma	II

CC: corpus callosum, CG: cingulate gyrus, I: insula cortex, L: left, M: motor area, MFG: middle frontal gyrus, R: right, SF: superior frontal gyrus, SMA: supplementary motor area, WHO: World Health Organization. In Patient 6, the SMA was resected in the first operation.

and IV, respectively). Detailed motor functions of each patient are shown in Table 2.

III. Operative protocols

Awake craniotomy was performed on patients under local anesthesia. After a dural incision, the motor cortex was evaluated using DES, which was delivered via a bipolar probe (5-mm tip) with a biphasic current (pulse frequency, 60 Hz; single-pulse phase duration, 1 ms; amplitude of biphasic current, 1–4 mA). Intraoperative tasks used in the awake craniotomy were as follows: object-naming; movement of the upper and lower extremities; working memory (2-back task); and visuospatial cognition (line bisection task). The upper extremity movement included flexion and extension of the elbow and fingers, and the lower extremity movement included flexion and extension of the knee. The upper limb movement and object-naming task were assessed simultaneously as a dual task. We continued monitoring movement and language during tumor resection. The same occupational therapist and speech therapist conducted the evaluation in all patients, and reported to the surgeon when they detected positive responses by DES. Tumor resection was continued until the DES defined positive mapping. The operative field and the scene of intraoperative evaluation were recorded using a video camera.

IV. Postoperative motor function

BRS was evaluated on the 3rd day, 7th day, and 3 months after surgery. Further evaluations were conducted where appropriate according to the

Table 2 Preoperative motor function and subsequent postoperative SMA syndrome

Patient	Preoperative motor symptom	Postoperative SMA syndrome		
		3 days	7 days	3 months
1	normal	yes	yes	no
2	normal	no	no	no
3	mild paresis	yes	no	no
4	mild paresis	yes	yes	mild paresis*
5	normal	yes	yes	no
6	normal	yes	no	no
7	mild paresis	yes	yes	no
8	normal	yes	yes	no

*: Equivalent to preoperative conditions. Presence of supplementary motor area syndrome (yes) was defined as the paresis newly occurred or exacerbated postoperatively.

recovery process. The presence of SMA syndrome was defined as motor weakness newly occurred or exacerbated postoperatively.

V. Analysis of video records

We analyzed six parameters using video records. These included the response to DES (as measured by negative motor responses or hypertonic responses); motor weakness (the presence or absence of the inability to continue the motor task); the delay of movement initiation (i.e., time until movement initiation after patients tried to start the movement or were told to start the movement by the occupational therapist); slowness of movement (the ratio of the required time for a reciprocal movement of the upper extremity, calculated as the speed at eruption of abnormal motor response divided by the speed before SMA resection); the difficulty in dual task response (success or failure of the dual task in the upper extremity movement and object-naming task); and coordination disturbance (success or failure of coordination movement of upper and lower limb or elbow and fingers).

Results

I. Operative findings

The depth of arousal was sufficient for the execution of the intraoperative tasks. Before the stimulations, the intraoperative tasks, which were identical to the preoperative tasks, were used to confirm that the initial motor and language functions were at the same level as those in the preoperative condition. DES to the cortical and subcortical regions, which were considered anatomically SMA proper, elicited negative motor responses (positive mapping) in all patients. The tumor resection was finished either when DES showed positive mapping or when the continuous voluntary movement monitoring became impossible due to characteristic motor symptoms. Figure 1 shows pre-, intra-, and postoperative images from two typical patients.

The details of motor symptoms during resection in every patient are shown in Table 3 and summarized below. Delayed motor weakness: in Patients 3 to 5, fingers and arm movements were impossible approximately 50 min, 60 min (30 min from the end of the SMA resection), and 90 min after the initiation of the SMA resection, respectively. Delay of movement initiation: Patients 3, 4, 5, and 8 showed delay in movement initiation of 1.5 s to 6.5 s. Of these, the delay in movement initiation for Patient 3 was observed just after awakening. In Patients 4, 5, and 8 delay of movement initiation occurred a few minutes after initiation of the

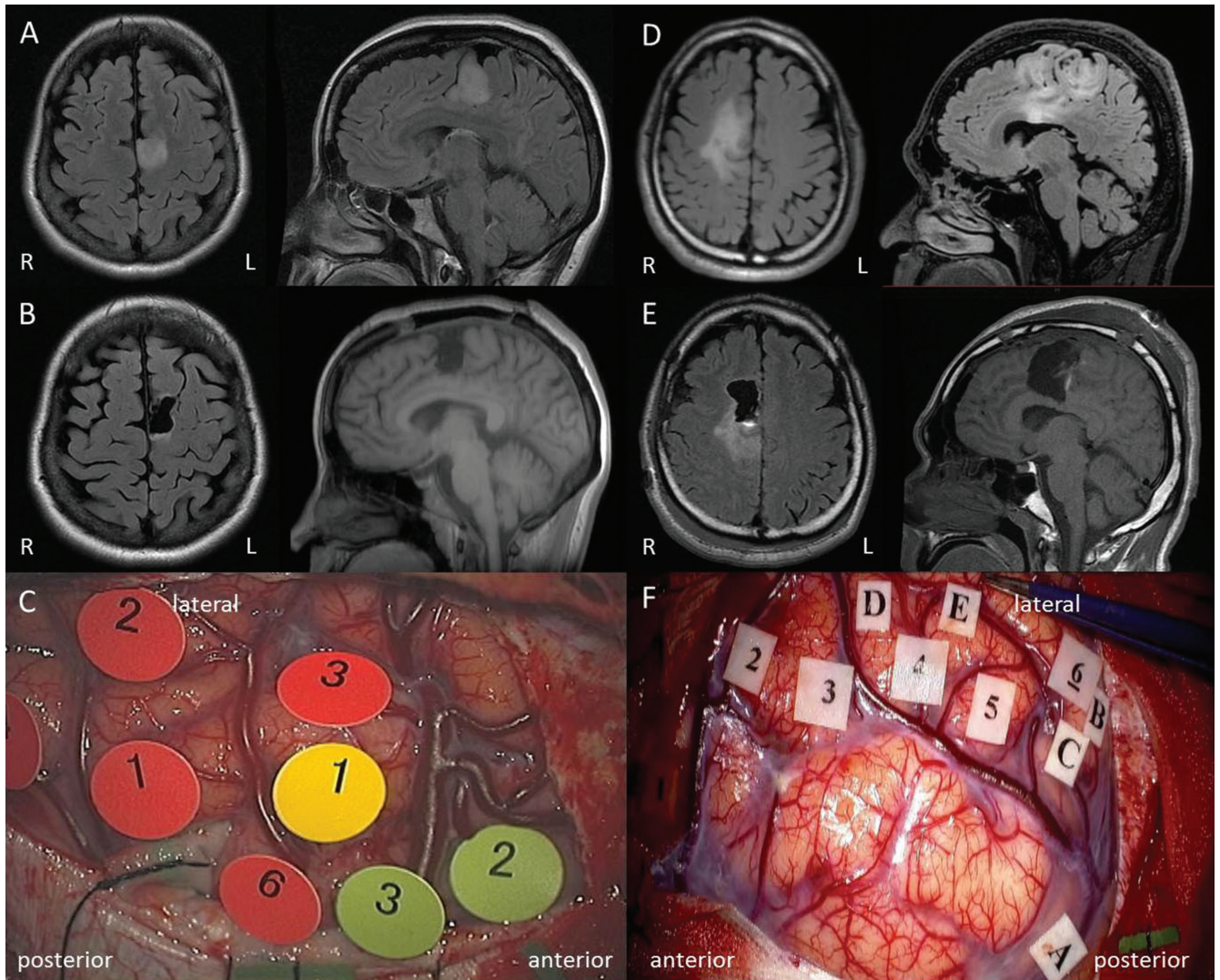


Fig. 1 Results of the imaging and functional mapping in Patients 1 (left panels, A–C) and 4 (right panels, D–F). **A:** Preoperative fluid-attenuated inversion recovery (FLAIR) magnetic resonance (MR) sagittal image shows a hypo-intense lesion in the left supplementary motor area (SMA). **B:** Postoperative T₁-weighted sagittal image shows a resection cavity located in the SMA, which does not extend to the cingulate gyrus below. **C:** Intraoperative picture shows functional mapping results; tags 1 (red) and 2 (red) indicate speech arrest and negative motor response, respectively. Tag 3 (red) indicates delayed response in the verbal 2-back task. Tag 6 (red) indicates preservation and mistake-response in the verbal 2-back task. **D:** Preoperative FLAIR MR sagittal image shows a hypo-intense lesion in the right SMA. **E:** Postoperative T₁-weighted sagittal image shows a resection cavity located in the SMA, extended to the cingulate gyrus below. **F:** Intraoperative picture shows functional mapping results; alphabet tags (tags A to E) indicate limits of the tumor predicted by an echography. The tag numbers 1 to 6 indicate areas eliciting negative motor response or hypertonic response following direct electrical stimulation (DES). L: left, R: right.

SMA resection. Slowness of movement (the reaction time of a single movement of the upper limb was 1.5 times longer compared to that before SMA resection); movement speed began to decrease during the SMA resection in Patients 4, 5, and 8, and this persisted until the end of the surgery in the awake condition. Difficulty in dual task response: the dual

task of object-naming and movement was impossible for Patients 3 to 6, and 8, and they could perform only one task at a time. Coordination disturbance: in Patients 1, 4, and 5 coordination movement of upper and lower limbs became unskillful during the SMA resection. Similarly, Patients 4 to 8 could not move elbow and fingers in a coordinated way.

Table 3 Summary of the intraoperative symptoms

Patient	Response to DES	Delayed motor weakness	Delay of movement initiation (s)	Reaction time of upper limb (s) before → after	Difficulty in dual task response	Coordination disturbance	Extent of resection
1	NMR	no	< 0.5	1.5 → 1.5	no	yes	GTR
2	NMR	no	< 0.5	0.8 → 0.8	no	no	GTR
3	NMR	Fin	2.5	1.0 → 1.0	yes	no	STR
4	NMR, HR	UE	1.5	0.8 → 5.2*	yes	yes	STR
5	NMR, HR	Fin	2.0–3.0	0.8 → 2.5*	yes	yes	STR
6	NMR, HR	no	< 0.5	0.8 → 0.9	yes	yes	STR
7	NMR	no	< 0.5	0.8 → 0.9	no	yes	STR
8	NMR, HR	no	1.5–6.5	1.6 → 6.8*	yes	yes	STR

*: Reaction time of single movement of upper limb was longer (> 1.5 times) compared with that before the SMA resection, after: after SMA lesion resection, before: before SMA lesion resection, DES: direct electrical stimulation, Fin: fingers, GTR: gross total resection, HR: hypertonic response, NMR: negative motor response, STR: subtotal resection, UE: upper extremity.

II. Postoperative course

Patients 3, 5, and 7 underwent chemotherapy and Patient 7 underwent radiotherapy. Patient 4 was moved to another affiliated hospital to continue rehabilitation. Within 3 months of the surgery, Patients 1, 2, 3, 6, and 7 returned to their previous social life. Seven patients (1, and 3 to 8) in whom intraoperative motor symptoms were observed showed contralateral hemiparesis immediately following the operation. On the other hand, Patient 2 with no intraoperative motor symptoms showed normal motor function postoperatively. As for the recovery to preoperative levels, Patients 3 and 6 required 1 week after surgery, and the other five patients required 2 weeks to 6 weeks. Thus, we report that postoperative hemiparesis in all patients recovered to preoperative levels within 6 weeks (Table 2). It is noteworthy that any patients did not show flaccid paresis, corresponding to BRS I, throughout the postoperative course, even with various symptoms of SMA syndrome. In neuropsychological tests immediately following the operation, Patient 3 showed transient aphasia, Patients 4 and 6 showed disordered spatial working memory, Patient 5 showed a disorder of fluency, and Patient 8 showed disordered visuospatial cognition and emotion. Furthermore, depression of processing speed and attention disorders were observed in all patients, but they recovered to near preoperative levels within 3 months of surgery.

Discussion

I. Intraoperative motor symptoms

This study revealed that various symptoms associated with function of the SMA were observed

during tumor resection of the SMA under awake conditions. Importance of continuous monitoring during tumor resection for preserving postoperative motor function is well known, and intraoperative abnormal motor symptoms may give warnings against continuing surgical resection.^{18,19)} As for resection of SMA lesion, intraoperative abnormal motor symptoms without positive mapping might be predictors for postoperative SMA syndrome, because SMA syndrome occurred in all patients in whom intraoperative motor symptoms were observed. Hence, even if these patients showed paralysis immediately after the operation, near complete recovery could be expected. In this regard, occurrences of intraoperative abnormal motor symptoms in region without positive mapping do not suggest definite warnings against continuing surgical procedure, since these symptoms do not predict permanent morbidities.

1. Delayed motor weakness

During tumor resection of the SMA we found that delayed motor weakness, thought to be associated with postoperative SMA syndrome, occurred more than 50 min later from the initiation of the SMA resection, and was not synchronized with initiation of SMA resection. Complete motor weakness of the upper extremity or fingers were found in three patients (3, 4, and 5) and occurred 50 min, 60 min (30 min after the end of SMA resection), and 90 min after the initiation of SMA resection, respectively. This finding was almost consistent with the report from Duffau et al. that showed that motor weakness, which was considered as part of the postoperative SMA syndrome, occurred 30 min after the SMA resection.²⁰⁾ Previous studies have

shown that motor weakness due to SMA syndrome was almost completely recovered within 3 months of surgery.^{10,21} In Patients 3, 4, and 5, recovery from hemiparesis occurred in the early postoperative period, suggesting their intraoperative delayed motor weakness would have been a symptom in predicting postoperative SMA syndrome.

2. Delay of movement initiation

Four patients showed delay of movement initiation between 1.5 s and 6.5 s. SMA is involved in the initiation of movement, and it coordinates the timing of the movement too.^{16,22–24} The delay of movement initiation found in this study was regarded as a symptom related to the SMA. In three of the four patients, the symptom occurred several minutes after the initiation of SMA resection. Therefore, the mechanism that results in the delay of movement initiation might differ from that which affects motor weakness, which occurs more than 50 min after the initiation of SMA resection.

3. Slowness of movement

The SMA plays a role in adjustment of movement speed and movement direction, and damage to the SMA is known to cause a reduction in movement speed.^{25,26} Movement speed appeared to decrease in three patients during the resection of the SMA. However, we cannot discount the possibility that the slowness of movement was based on delayed motor weakness. Therefore, detailed studies based on native function of the SMA are required to differentiate between conditions.

4. Difficulty in dual task response

Difficulty in dual task response was observed in five of eight patients. In a dual task of movement and language, the SMA was activated more significantly compared to the single task assessing movement only.²⁷ The SMA also adjusts movements temporally and programs self-paced movement rhythm.^{23,24} The intraoperative dual task we used in this study was a simultaneous assessment of spontaneous continued movement of the arm and a language task. Our results suggest that the SMA plays a functional role in completing the two different tasks concurrently. Furthermore, depending on extraction regions, single task monitoring should be used because the difficulty of dual task response affects the absolute evaluation of the movement and language function.

5. Coordination disturbance

SMA plays an important role in coordination movement of interlimb, bilateral hands, and upper and

lower limbs.^{15,28–30} Six patients could not move upper and lower limbs or elbow and fingers in a coordinated manner synchronously with SMA resection. Since coordination disturbance was the symptom not explained by other motor symptoms, such as disorder of movement initiation or dual task response, it can be understood as one of the characteristic intraoperative abnormal motor symptoms. Overall, recognition of various reversible motor symptoms resulting from SMA function is important for judging the continuation of surgical resection in an awake surgery.

II. Postoperative recovery following intraoperative motor symptoms

Three patients showed intraoperative delayed motor weakness followed by severe to mild postoperative hemiparesis but they recovered to preoperative levels within 6 weeks. Therefore, consistent with previous reports about SMA syndrome,^{3,10,21,31} delayed motor weakness, thought to originate in the SMA, can be nearly completely recovered during postoperative course. The mechanism underlying the delayed motor weakness was unclear. Complex interactions of functional networks, including the fronto-striatal tract and the frontal aslant tract, which is related to the SMA region, could have induced these particular motor symptoms.^{32,33} In one patient (case 4, Fig. 1, right panels D–F), the motor functions recovered to the preoperative level, but mild paresis persisted. In this case, resection of the cingulate gyrus with SMA could have played a causal role in the persistent paresis in addition to the tumor invading the primary motor cortex.³⁴ Moreover, in three patients in whom delayed motor weakness was observed, three showed precursory delay of movement initiation, and two showed precursory slowness of movement. Since we could not determine the relationship between the onset of these motor symptoms and mechanism in this study, further studies are required.

Delay of motor initiation and slowness of movement occurred within several minutes after tumor resection of the SMA. As mild motor weakness can also be caused by motor cortex or pyramidal tract injuries, we needed to meticulously distinguish between the symptoms derived from the SMA resection and those coming from motor cortex or pyramidal tract injuries.^{6,18,35} In this respect, continuous monitoring, including careful attention to intraoperative motor symptoms, such as delay of movement initiation, and slowness of movement, is essential in order to make proper judgments during an awake surgery of the SMA.

III. Awake surgery and DES during SMA tumor resection

The awake surgery is an effective method to avoid permanent morbidities, and intraoperative continuous motor monitoring, with appropriate evaluations of various movement symptoms, would lead to improvements in the indications of the awake surgery.

The usefulness of awake surgery for SMA lesions is still debatable because the normal recovery of the postoperative SMA syndrome can lead to unnecessary intraoperative mapping. Nonetheless, even if rare cases with deficits which may not impair the daily activities, patients with permanent disabilities after resection of the sole SMA lesion, SMA proper rather than pre-SMA, have been reported,^{36–39)} and the mechanism of recovery is unclear. Thus, the possibility of permanent morbidities cannot be ruled out in any of the cases. Further, even faint disabilities can affect the patient's professional life. Although the etiologies of the permanent morbidities are unclear, recent network studies have indicated that several important functional networks exist in relation with the SMA.^{32,33)} From the point of view of the "minimal common brain," these network functions are more important for functional preservation.⁴⁰⁾ To evaluate network function, awake surgery with cortical and subcortical mapping is a suitable surgical modality. Nonetheless, evaluation of network function is beyond the scope of the present study, and the present data were not obtained to evaluate network function. The data were from the surgical procedures that were performed with our safe surgical criteria with which positive mapping regions should be preserved. In terms of establishing safe surgeries, increasing the documented experiences with intraoperative mapping during SMA tumor resection should be useful for evaluating the functional network relative to SMA and for elucidating the mechanism underlying SMA syndrome.

In the present patient group, regions presenting DES-induced negative motor responses (positive mapping area) were left unresected, and we determined these regions as the excision limit of the tumor. As a result, tumor remnants were present in the SMA proper. Previous reports suggested that regions with DES-induced negative motor responses could anticipate near complete recovery after the resection.^{20,21,41)} Meticulous observations of motor-evoked potentials (MEPs) with subdural electrodes have indicated that single-pulse electrical cortical stimulation can be useful for distinguishing SMA from primary motor cortex.⁴²⁾ However, during awake surgery without MEP monitoring, it could be technically difficult to distinguish the SMA proper which is responsible for negative motor response by

DES from the close locating primary motor cortex which could be also responsible for motor arrest that occurs in the silent period immediate after momentary positive motor response by DES. In addition, high-frequency stimulation during awake surgery tends to induce negative motor responses that are related to apraxia of fine movements.⁴³⁾ More precise evaluation methods including dual monitoring with DES and MEP will be needed in the future to determine whether DES-induced negative motor responses are derived from the SMA.

IV. Limitations of this study

Because of the limited number of patients in this study, we could not find a correlation between the degree of intraoperative motor symptoms and the severity of postoperative symptoms. Moreover, previous reports indicated that the body region with postoperative SMA syndrome corresponded to the somatotopy of the SMA.^{3,44,45)} Common anatomical features, however, could not be found in the body regions related to delayed motor weakness or delay of movement initiation in this study.

Conclusion

The following characteristic motor symptoms were observed during tumor resection of the SMA in awake condition, even in area without positive mapping by DES: delayed motor weakness, delay of movement initiation, slowness of movement, difficulty in dual task response, and coordination disturbance. Although the prognosis is generally considered favorable, patients who would undergo an awake surgery for SMA lesions should be informed of these particular motor symptoms, and the surgeon also should recognize these intraoperative motor symptoms during resection of region without positive mapping could be reversible. Although the usefulness of awake surgery for SMA lesion is still in debate, to increase documented experience with intraoperative mapping during SMA tumor resection and to delineate its role in an overall management paradigm should be important for a safe surgery.

Conflicts of Interest Disclosure

The authors have no personal, financial, or institutional interest in any of the materials or devices described in this article.

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