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Current Status and Future Objectives of Surgical Therapies for Epilepsy in Japan

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Abstract

This study investigated the number of epilepsy surgeries performed over time in Japan, and conducted a questionnaire survey of the Japan Neurosurgical Society (JNS) training program core hospitals to determine the current status and future objectives of surgical therapies and epilepsy training programs for physicians in Japan. This article presents part of a presentation delivered as a presidential address at the 44th Annual Meeting of the Epilepsy Surgery Society of Japan held in January 2021. The number of epilepsy surgeries performed per year has increased in Japan since 2011 to around 1,200 annually between 2015 and 2018. The questionnaire survey showed that 50% of the responding hospitals performed epilepsy surgery and 29% had an epilepsy center, and that these hospitals provided senior residents with education regarding epilepsy surgery. The presence of an epilepsy center in a hospital was positively correlated with the availability of long-term video electroencephalography monitoring beds as well as the number of epilepsy surgeries performed at the hospital. In regions with no medical facilities offering specialized surgical therapies for epilepsy, the JNS training program core hospitals may help improve epilepsy diagnosis and treatment. They may also increase the number of safe and effective surgeries by establishing epilepsy centers that can perform long-term video electroencephalography monitoring, providing junior neurosurgeons with training regarding epilepsy, and playing a core role in surgical therapies for epilepsy in tertiary medical areas in close cooperation with neighboring medical facilities.

Keywords: epilepsy surgery, long-term video electroencephalography monitoring

Introduction

A Japanese academic society for epilepsy surgery was originally founded as the W. Penfield Memorial Symposium in 1978. Its name was changed to the

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Epilepsy Surgery Society of Japan in 2000, and the society has held an annual meeting since then. No recent studies have reported the number of epilepsy surgeries in Japan or the future objectives related to these procedures; in contrast, there have been many reports on the numbers of these surgeries in other countries. This article reports part of a presentation delivered as the presidential address, including the subsequent discussion, delivered at the 44th Annual Meeting of the Epilepsy Surgery Society of Japan in January 2021. It discusses the current status and future objectives of surgical therapies and physician training programs for epilepsy in Japan.

Methods

The number of epilepsy surgeries in Japan was investigated based on the annual reports of the Japan Neurosurgical Society (JNS; 2001–2018) on total number; the National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB; 2014–2018)[1] on focus resection, temporal lobectomy, and corpus callosotomy; and the Japan Neurosurgery Registry (2015–2017) on subdural electrodes depending on the data collection method. Since the number of total epilepsy surgery and corpus callosotomy was overlapping between reports, longer continuous data from JNS and NDB were chosen respectively.

In addition, we mailed a questionnaire (Table 1) on the management of epilepsy, including its surgical treatment, to 95 JNS training program core hospitals.

Statistical analysis

Fisher's exact probability tests and χ^2 tests were used to compare responses between JNS training program core hospitals with and without epilepsy centers. Values of $p < 0.05$ were considered statistically significant. All statistical analyses were performed with JMP Pro 15 software (SAS Institute, Cary, NC, USA).

Results

According to the annual reports of the JNS, the yearly number of epilepsy surgeries in Japan has increased since 2011 to around 1,200 per year between 2015 and 2018; this includes around 400 vagus nerve stimulation (VNS) implantation surgeries (Fig. 1). According to the NDB, the most common surgery for epilepsy was focus resection. The number of temporal lobectomy surgeries has decreased over time, and in 2017, it was comparable to that of corpus callosotomy surgeries. In 2018, the number of corpus callosotomy surgeries surpassed that of temporal lobectomy surgeries (Fig. 2). We conducted a questionnaire survey on the management of epilepsy and its surgical treatment. Of 95 JNS training program core hospitals that were sent a questionnaire by mail, 90 (95%) responded. Regarding equipment related to epilepsy diagnosis (Fig. 3), all facilities were equipped with a digital electroencephalograph. Thirteen facilities were equipped with a magnetoencephalography scanner and 40 were equipped with long-term video electroencephalography monitoring beds. The number of these beds in general wards was one in 16 facilities, two in 12 facilities, and three or more in 12 facilities; the number in intensive care units was one in 16 facilities and two in two facilities, while no facilities had three or more. The total number of these beds in general wards and intensive care units was 110. Figure 4 shows the types of medical care available in neurosurgery departments for patients with epilepsy.

The number of epilepsy surgeries per year was ≥30 at 11 facilities, 20 to <30 at five facilities, 10 to <20 at seven facilities, 1 to <10 at 22 facilities, and 0 at 45 facilities (Fig. 5). The number of VNS implantation surgeries was ≥30 at one facility, 20 to <30 at one facility, 10 to <20 at four facilities, 1 to <10 at 32 facilities, and 0 at 52 facilities. Seventy-four facilities reported that their neurosurgery departments interpreted the electroencephalograms of patients with epilepsy. The numbers of facilities that submitted orders for electroencephalogram interpretation when necessary to neurology, pediatrics, or psychiatric departments were 25, 18, and 10, respectively. Figure 6 shows the types of epilepsy-related training that facilities provided to medical students and/or residents. In terms of the training provided to medical students, junior residents, and senior residents, senior resident training was the most commonly available, followed by medical student training. In particular, training on electroencephalogram interpretation and pharmacologic treatment was provided during senior resident training. Few facilities provided no such opportunities at all. However, the number of facilities that provided opportunities to learn about epilepsy at academic meetings exceeded the number of facilities that provided such opportunities during senior resident training.

Twenty-six (29%) facilities responded that they had an epilepsy center. The total number of epilepsy surgeries ($p < 0.0001$) and the number of VNS implantation surgeries ($p < 0.0001$) were significantly higher at facilities with an epilepsy center compared to those without. Similarly, regarding equipment

Table 1 Questionnaire on the management of epilepsy in the neurosurgery department

1: What equipment related to epilepsy diagnosis does your facility have? (Select all that apply.)

1. Electroencephalograph (analog)
2. Electroencephalograph (digital)
3. Single photon emission computed tomography (SPECT) scanner
4. Positron emission tomography (PET) scanner
5. Magnetoencephalography (MEG) scanner
6. The number of beds that can be used for long-term video electroencephalography monitoring (General ward: _____beds; ICU _____beds)

2: How many outpatients with epilepsy does your neurosurgery department see per week? (including both initial and subsequent visits)

1) Partial epilepsy

1. 0 2. <1 3. 1 to <10 4. 10 to <30 5. ≥30

2) Generalized epilepsy

1. 0 2. <1 3. 1 to <10 4. 10 to <30 5. ≥30

3: Does your facility have an epilepsy center?

1. Yes 2. No

4: How many epilepsy surgeries does your neurosurgery department perform per year?

1) The number of surgeries per year

1. 0 2. 1 to <10 3. 10 to <20 4. 20 to <30 5. ≥30

2) How many vagus nerve stimulator implantation surgeries are included in the number of surgeries referred to in 1) above?

1. 0 2. 1 to <10 3. 10 to <20 4. 20 to <30 5. ≥30

5: What kinds of medical care are available for patients with epilepsy in your neurosurgery department? (Select all that apply.)

1. Emergency medical care
2. Medication for patients whose epileptic seizures have already stopped
3. Medication for patients with persistent epileptic seizures
4. Initial diagnosis of epilepsy based on patient interviews, electroencephalography, and MRI scans
5. Diagnosis of epilepsy based on video electroencephalogram monitoring during a seizure
6. Intracranial electrode implantation surgery (subdural or deep electrode)
7. Vagus nerve stimulator implantation surgery
8. Adjustment of implanted vagus nerve stimulator

6: Please select all that apply regarding partnerships for epilepsy medical care between your neurosurgery department and other clinical departments in your facility or other facilities in the community

1. We cooperate with other clinical departments in our facility
2. We cooperate with other facilities in the community
3. We have a regional medical network system in the community
   (Specify the name of the system:)
4. We recognize the need for a regional partnership but do not have it
5. We do not think that a regional partnership is needed
6. Other (Specify:)

Table 1 (Continued)

7: What kinds of remote medical care does your neurosurgery department provide? (Select all that apply.)

1. Doctor to patient (online medical care)
2. Doctor to doctor (remote electroencephalogram interpretation)
3. Doctor to doctor (case study meetings)
4. Doctor to doctor to patient (remote collaborative medical care using information technology)
5. No remote medical care is provided
6. Other (Specify:)

8: What persons or departments are responsible for interpreting electroencephalograms of patients with epilepsy who receive medical care in your neurosurgery department? (Select all that apply.)

1. Neurosurgery department
2. Order for interpretation is submitted to the neurology department of our facility
3. Order for interpretation is submitted to the pediatrics department of our facility
4. Order for interpretation is submitted to the psychiatric department of our facility
5. Online order for interpretation is submitted to an external facility
6. Patients visit an external doctor or an order for interpretation is mailed to an external doctor

9: What opportunities does your facility provide for neurosurgeons to acquire knowledge regarding the following epilepsy-related topics? (Select all that apply.)

1) Diagnosing epilepsy seizure types (using videos as learning materials)

1. In neurosurgery lectures for medical students
2. During junior resident training
3. During senior resident training (for neurosurgery)
4. At academic meetings and/or workshops
5. No opportunities are provided

2) Interpreting electroencephalograms of patients with epilepsy

1. In neurosurgery lectures for medical students
2. During junior resident training
3. During senior resident training (for neurosurgery)
4. At academic meetings and/or workshops
5. No opportunities are provided

3) Interpreting MRI data of patients with epilepsy (for diagnosis of hippocampal sclerosis and focal cortical dysplasia)

1. In neurosurgery lectures for medical students
2. During junior resident training
3. During senior resident training (for neurosurgery)
4. At academic meetings and/or workshops
5. No opportunities are provided

4) Pharmacologic treatment of epilepsy

1. In neurosurgery lectures for medical students
2. During junior resident training
3. During senior resident training (for neurosurgery)
4. At academic meetings and/or workshops
5. No opportunities are provided

5) Epilepsy surgery

1. In neurosurgery lectures for medical students

Table 1 (Continued)

2. During junior resident training
3. During senior resident training (for neurosurgery)
4. At academic meetings and/or workshops
5. No opportunities are provided

10: How should basic education regarding epilepsy medical care be provided as part of career-long training for neurosurgeons? (Select all that apply.)

1. It should be provided in neurosurgery lectures for medical students
2. It should be provided during junior resident training
3. It should be provided during senior resident training (for neurosurgery)
4. It should be provided at academic meetings and/or workshops
5. No change to the current education system is needed

11: What drug is used for the Wada test in your neurosurgery department?

1. Amobarbital
2. Methohexital
3. Isozol
4. Propofol
5. The Wada test is not performed

Please answer the questions below based on your personal opinion:

12: Do you think that a neurosurgeon should interpret electroencephalograms of patients with epilepsy when their electroencephalography examination is ordered by the neurosurgery department?

1. Yes **Go to Question 13**
2. No **Go to Question 14**

13: Please answer this question only if you answered "Yes" to Question 11.

What medical care for epilepsy should neurosurgeons provide based on a neurosurgeon's diagnosis? (Select all that apply.)

1. Differential diagnosis of epilepsy and epilepsy subtypes
2. Medication
3. Surgical treatment

14: Please answer this question only if you answered "No" to Question 11.

What medical care for epilepsy should neurosurgeons provide based on electroencephalograms interpreted by a specialist in another clinical department?

1. No medical care except emergency care
2. Medication should be administered but surgery should not be performed
3. Medication should be administered and surgery should be performed

15: Some think that the number of epilepsy surgeries in Japan is insufficient compared with that in Western countries. What measures do you think should be taken to improve this situation?

1. None (maintain the status quo)
2. Educate neurosurgeons
3. Strengthen interprofessional cooperation
4. Establish a regional medical network system

Table 1 (Continued)

16: It has been reported that the average number of epilepsy surgeries in Japan is approximately 1,000 annually (Japan Neurosurgery Registry, NMC 2019). What factors do you think are important regarding the education of neurosurgeons who will be responsible for future epilepsy surgery?
1. Training on techniques for epilepsy microsurgery
2. Training on surgical techniques (vagus nerve stimulation, responsive neurostimulation) other than craniotomy
3. Training on surgical techniques (deep brain stimulation) other than craniotomy
4. Training on surgeries other than epilepsy surgery
5. Other (Specify:)

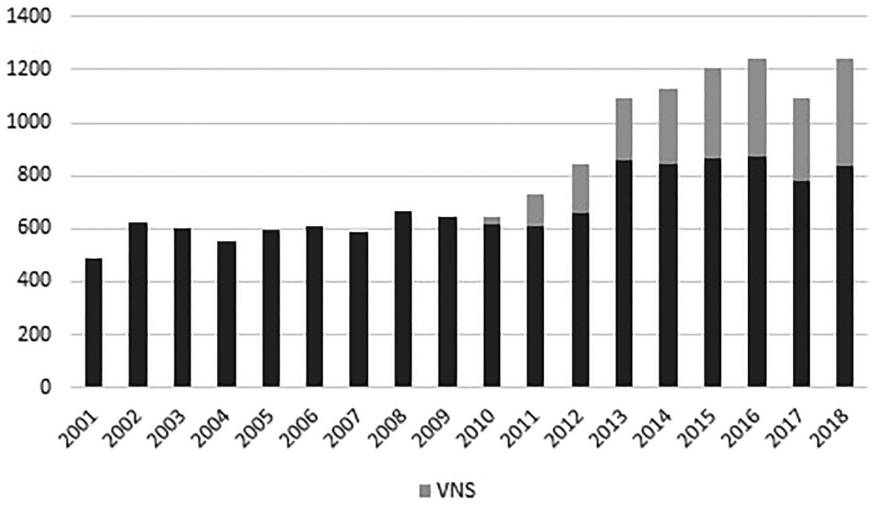

Fig. 1 Number of annual epilepsy surgeries from 2001 to 2018 according to the annual reports of the JNS. The number of epilepsy surgeries performed per year was approximately 600 until 2010. Since VNS was introduced into clinical practice in 2011, the numbers of both VNS implantation surgeries and other types of surgeries have increased. Since 2015, the total annual number of epilepsy surgeries has been around 1200. JNS: Japan Neurosurgical Society, VNS: vagus nerve stimulation.

related to epilepsy diagnosis, there was a correlation between the presence of an epilepsy center and the availability of magnetoencephalography ($p = 0.0018$) and long-term video electroencephalography monitoring beds ($p = 0.0003$).

Discussion

The annual number of epilepsy surgeries in Japan was approximately 600 until 2010, after which it began to increase, reaching around 1200 beginning in 2015. Since VNS was introduced into clinical practice, approximately 400 VNS surgeries have been performed per year. Thus, the annual number of non-VNS-related craniotomy surgeries for epilepsy has also increased, by approximately 200. The reason for this increase may be that the introduction of VNS for the treatment of drug-resistant epilepsy has raised awareness of epilepsy surgery, resulting in an increased number of referrals to epilepsy centers. Also, surgical therapies have come to be indicated for a wider range of patients with epilepsy. In terms of specific surgical techniques, the annual number of temporal lobectomies decreased in the 5 years beginning in 2014, even though the Japanese clinical guidelines for epilepsy management[2] state, "The efficacy and safety of temporal lobectomy in patients with drug-resistant temporal lobe epilepsy has been established and should be considered for patients with complex partial seizure that interferes with daily activities." The decrease in the number of surgeries for temporal lobe epilepsy is consistent with reports from major overseas epilepsy centers,[3–6] suggesting the possibility of a decrease in the number of patients with epilepsy as well as the efficacy of novel antiepileptic drugs.

The number of epilepsy surgeries per year in the United States, which has a population of 330.06 million (as of January 2021 according to the United States Census Bureau), was 3239 in 2008 and 2913

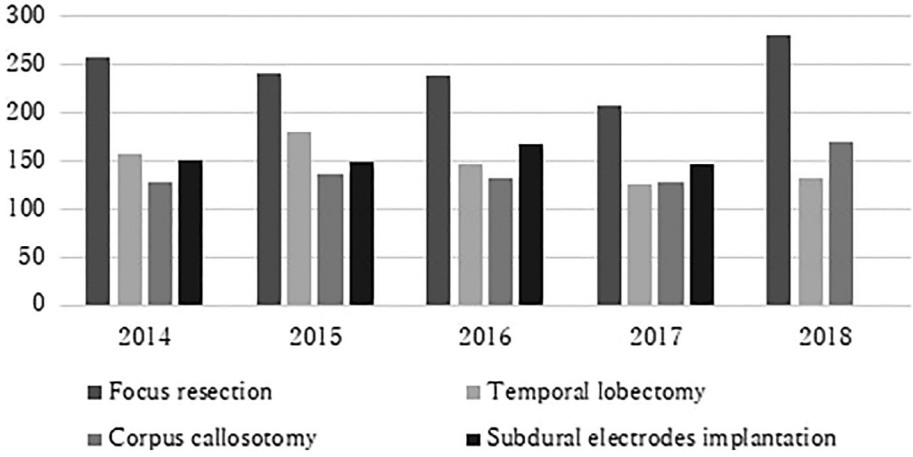

Fig. 2 Number of each type of epilepsy surgery performed annually from 2014 to 2018 according to the annual reports of the NDB and JND. In recent years, focus resection has been the most common epilepsy surgery, with over 200 performed per year. The annual number of temporal lobectomy surgeries has decreased over time, becoming similar to the number of corpus callosotomy surgeries and falling below the numbers of subdural electrode implantation surgeries performed in 2016 and 2017. Note that the number of subdural electrode implantation surgeries in 2018 is unknown. JND: Japan Neurosurgical Database, NDB: National Database of Health Insurance Claims and Specific Health Checkups of Japan.

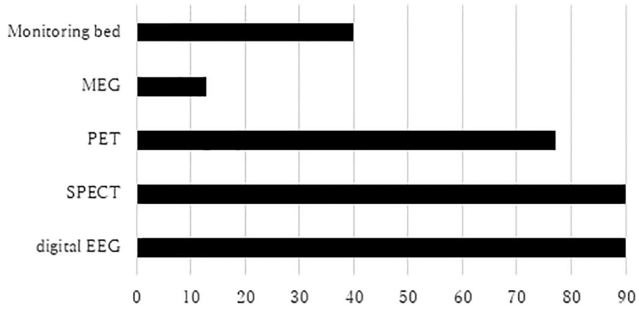

Fig. 3 Epilepsy diagnosis-related equipment at 90 JNS training program core hospitals. JNS: Japan Neurosurgical Society, Monitoring bed: long-term video electroencephalography monitoring bed, MEG: magnetoencephalography, PET: positron emission tomography, SPECT: single photon emission computed tomography, EEG: electroencephalography.

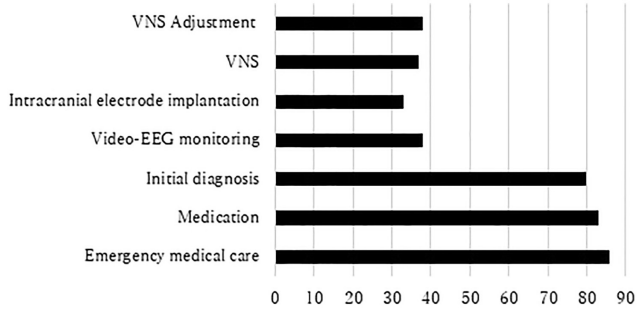

Fig. 4 Medical care available in neurosurgery departments for patients with epilepsy. VNS: vagus nerve stimulation, EEG: electroencephalography.

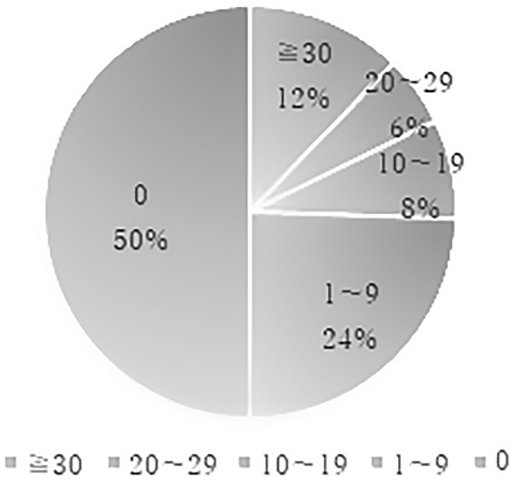

Fig. 5 Number of epilepsy surgeries performed annually at 90 JNS training program core hospitals. Each upper number in the graph indicates the number of epilepsy surgeries (≥30, 20–29, 10–19, 1–9, 0) performed annually at each facility, and each lower number indicates the percentage of the 90 facilities. JNS: Japan Neurosurgical Society.

in 2012.[7] The number in Japan, with a population of 125.57 million, was approximately 1200. Therefore, the number per population in the United States and in Japan was similar. In the United States, future objectives focus on referring the maximum possible number of patients with drug-resistant epilepsy to full-service epilepsy centers. It has been reported that the prevalence of epilepsy in the

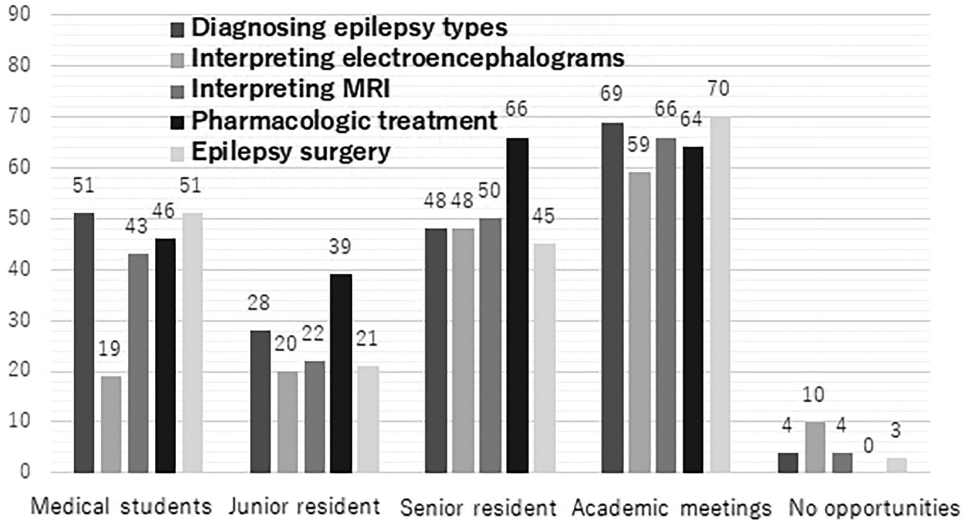

Fig. 6 Diagnosing epilepsy seizure types, interpreting electroencephalograms and MRIs, and pharmacologic treatment. Types of training provided to neurosurgeons by JNS training program core hospitals for acquiring knowledge regarding epilepsy-related topics. MRI: magnetic resonance imaging, JNS: Japan Neurosurgical Society.

general population is approximately 1%, approximately 30–40% of patients with epilepsy are drug resistant, and epilepsy surgery is safe and effective for these patients.[8–10] However, only 36% of patients with drug-resistant epilepsy undergo a comprehensive epilepsy evaluation[11] and less than 1% of patients with epilepsy are referred to full-service epilepsy centers to be assessed for surgical eligibility.[11–13] Furthermore, it has been reported that only 1–2% of patients with drug-resistant epilepsy ultimately undergo surgery, and some of them are referred to low-volume, non-academic hospitals where treatment outcomes are worse and complication rates are higher.[14] Therefore, one study recommended that in order to provide many more patients with refractory epilepsy with safe and effective surgical therapy, the number of referrals to full-service epilepsy centers offering specialized diagnosis and other alternative treatments, as well as psychosocial support, should be increased.[13] Regarding this recommendation, we consider the following based on the results of this study. Important roles of the JNS training program core hospitals include promoting equal accessibility to neurosurgical care in the community and providing resident physicians with relevant training. This study revealed that among JNS training program core hospitals that responded to the questionnaire, 50% performed epilepsy surgery and 29% had an epilepsy center, and that these hospitals provided senior residents with education regarding epilepsy surgery. It also revealed that the presence of epilepsy center at a facility was positively correlated with the availability of long-term video electroencephalography monitoring beds as well as with the number of surgeries. The JNS training program core hospitals provide a training program that is required for physicians to become board-certified neurosurgeons. In this regard, these hospitals are well supported by the relevant subspecialty societies of the JNS. Physicians who wish to be board-certified neurosurgeons must meet the criteria for the board certification program, including having adequate surgical experience, but if they have no opportunity to participate in surgeries at the facility where they are trained, they can fulfill the criteria by observing surgeries at other medical facilities. It is not realistic for all core hospitals to rapidly establish full-service epilepsy centers that can also provide psychosocial support. However, as core hospitals in tertiary medical areas, it may be possible for them to have epilepsy centers that are equipped with beds that can be used for long-term video electroencephalography monitoring, which will allow for accurate epilepsy diagnosis, adjustment of antiseizure medications, and an accurate assessment of whether surgery is indicated for each patient.[15–18]

In regions with no JNS training program branch hospitals or related hospitals that can provide specialized surgical treatment for epilepsy, the JNS training program core hospitals may contribute to improving the quality of diagnosis and treatment of epilepsy and increasing the number of safe and effective surgeries by establishing epilepsy centers,

closely cooperating with neighboring hospitals, and providing junior neurosurgeons with epilepsy-related training. By establishing an epilepsy center and deepening cooperation with neurology, pediatrics, and psychiatry through case conferences and propaganda, it is expected that the role of the epilepsy center will develop.

In Japan, the more widespread use of stereotactic electroencephalography, as well as the introduction of new surgical therapies such as the responsive neurostimulator system (RNS System; NeuroPace, Inc., Mountain View, CA, USA), laser ablation (Visualase MRI-guided Laser Ablation System; Medtronic, Minneapolis, MN, USA), and deep brain stimulation, is expected to contribute to increasing the number of patients with epilepsy who can be treated surgically in the near future.[19–21]

Conclusion

The presence of an epilepsy center in a hospital was positively correlated with the availability of long-term video electroencephalography monitoring beds as well as the number of epilepsy surgeries performed at the hospital. In regions with no medical facilities offering specialized surgical therapies for epilepsy, the JNS training program core hospitals may help improve epilepsy diagnosis and treatment. They may also increase the number of safe and effective surgeries by establishing epilepsy centers that can perform long-term video electroencephalography monitoring, providing junior neurosurgeons with training regarding epilepsy, and playing a core role in surgical therapies for epilepsy in tertiary medical areas in close cooperation with neighboring medical facilities. Training in new surgical techniques is important for both young and experienced neurosurgeons who perform epilepsy surgery. Therefore, this is an important time for the JNS training program core hospitals to establish a new system for epilepsy surgery.

Acknowledgment

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Conflicts of Interest Disclosure

All authors declare that there are no conflicts of interest (COIs) regarding this article according to the criteria of the JNS. They completed the self-reported registration of their COI status to the society.

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