



Neuronavigation-assisted surgical treatments for medically refractory epilepsy: Single-hospital experience with 4 surgical approaches

Jia-Sheng Pei^a, Peng-Fan Yang^{a,*}, Qiao Lin^b, Yan-Zeng Jia^b, Hui-Jian Zhang^a, Ming-Chao Shang^a, Zhong-Hui Zhong^b, Shou-Sen Wang^a

^a Department of Neurosurgery, Fuzhou General Hospital, Fujian Medical University, Fuzhou, 350025, China

^b Department of Epileptology, Fuzhou General Hospital, Fujian Medical University, Fuzhou, 350025, China

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ABSTRACT

Objective: Surgical treatment should be considered for patients with medically refractory epilepsy, and neuronavigation may benefit and reduce the technical difficulties during surgery. In this study, we aimed to report our single-hospital experience of incorporating neuronavigation for treating patients with medically refractory epilepsy using 4 types of surgery.

Patients and methods: Patients who were diagnosed as medically refractory epilepsy and received neuronavigation-assisted surgery were included in this retrospective analysis. The type of surgery was decided by the surgery committee after careful evaluation and discussion, including temporo-parietal-occipital (TPO) disconnection, anterior subtotal callosal section, functional hemispherectomy and resection of the epileptogenic zone(s). Postoperative seizure outcome at the last visit was evaluated using Engel classification.

Results: A total of 173 patients with medically refractory epilepsy who were treated surgically under the assistance of neuronavigation were included. The majority type of surgery was resection of epileptic zone, $n = 104$ (60.12%). An excellent seizure outcome, Engel Class I was found in 50.86% of the patients, followed by 23.12% patients with a good outcome of Engel Class II.

Conclusion: Overall more than half of the patients could have excellent seizure outcome of Engel Class I, the postoperative complications were manageable. These results indicated that the applicability of neuronavigation, and the use of neuronavigation provides good efficacy and safety for all kinds of surgical procedures for patients with medically refractory epilepsy.

1. Introduction

Many patients with epilepsy could have good prognosis of achieving seizure-freedom with antiepileptic drugs. However, up to 30% patients still have seizure despite adequate treatment with at least 2 kinds of antiepileptic drugs, they are defined as medically refractory epilepsy [1,2]. Surgical treatment should be considered for these patients to achieve seizure-freedom or to obtain significant seizure reduction. A Practice Parameter published in 2003 has recommended surgery as the treatment of choice for medically refractory epilepsy [3]. A population-based study analyzed the data from a Nationwide Inpatient Sample from 1988 to 2003, among patients with medically refractory epilepsy treated by anterior temporal lobectomy, the results indicated that postoperative morbidity was 8% and a total overall morbidity of 10.8%, while the mortality rate was 0% [4]. However, surgery for treating

patients with medically refractory epilepsy is still underutilized. Less than 1% of patients with medically refractory epilepsy in United States were referred to undergo presurgical evaluation and surgery [5,6].

Resistance to surgery may be due to the epileptogenic region cannot be identified before the dura was opened, and the concern of the severe postoperative morbidity and mortality in the past [7]. In fact, in recent decades, great improvement of neuroimaging has increased the efficacy and safety of neurosurgery. For medically refractory epilepsy, the improved efficacy and safety were proved by a randomized controlled trial [8]. The mortality rate of patients with medically refractory epilepsy is about 4–7 times higher than that of the general population. Therefore, the more understandings on how the improvements of neuroimaging and surgical techniques for epilepsy surgery contribute to extension of lifespan and quality of life in these patients [9,10]; the more encouraging it is for patients to be treated medically refractory epilepsy

* Corresponding author at: Department of Neurosurgery, Fuzhou General Hospital, Fujian Medical University, North Road 156, West Second Ring, Fuzhou, 350025, China.

E-mail address: pfyang0511@126.com (P.-F. Yang).

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surgically as early as possible.

Neuronavigation is a set of computational process that allows co-registration of pre- and/or intraoperative images and patient anatomy, aids the image-guided neurosurgery [11,12]. Neuronavigation systems provides good spatial orientation, can be used preoperative, intraoperative, or real-time imaging with the accuracy of 2–5 mm [13,14]. Epilepsy surgery, similar to other neurosurgical procedures, can be aided by neuronavigation, which provides anatomical guidance for complete resection or disconnection with minimal invasion approach and maximal preservation of neural functions. In this study, we aim to report our single-hospital experience of using neuronavigation to treat medically refractory epilepsy patients with 4 types of surgery.

2. Patients and methods

2.1. Patients

Between September 2008 and April 2017, a total 2198 patients with epilepsy underwent surgery in our department. Patients who were diagnosed as medically refractory epilepsy, received surgery assisted by neuronavigation and followed-up for at least 12 months were included in this retrospective analysis. Neuronavigation-guided surgery was performed in patients who present with cortex lesions adjacent to eloquent areas, with small lesions in the deep of the cerebral sulcus, with lesions having undefined resection margins, with anatomic variations, or patients who underwent the dissection in the substantia alba at the deep of hemisphere, which clearer guidance is required by the surgeons. The study was approved by the Institutional Review Board of Fuzhou General Hospital (No. 2017-7-23). The diagnosis of medically refractory epilepsy was based on the proposal by the International League Against Epilepsy [2]. All patients underwent intensive pre-surgical evaluation, including cranial computed tomography (CT) scanning, magnetic resonance imaging (MRI) including, susceptibility-weighted imaging (SWI) sequences, and long-term video-electroencephalography (EEG). Positron emission tomography (PET/CT) were performed in selected patients, for example in patients with intractable or temporal epilepsy to examine metabolic changes.

The type of surgery was decided by the surgery committee after careful evaluation and discussion. Temporo-parietal-occipital (TPO) disconnection was offered when patients had focal seizures with unilateral TPO onset or generalized seizures with asymmetric clinical or EEG features suggesting a regional or extensive basis in unilateral TPO region. MRI or functional imaging should show abnormality in the ipsilateral TPO region [15]. Anterior subtotal callosal section (splenium was spared) was suggested when patients have drop attack, generalized seizures but were not suitable for focal resection and for patients with refractory frontal lobe seizures that cannot be adequately localized [16,17]. Functional hemispherectomy was considered for patients with widespread epileptogenic zone in unilateral hemisphere and contralateral hemiparesis [18]. Resection of epileptogenic zone(s) was performed when it/they could be identified and was resectable.

2.2. Neuronavigation

StealthStation Surgical Navigation System (Medtronic, Minneapolis, MN, USA) was used for preoperative planning and intraoperative guidance. Anatomical marker points (e.g. nasal, orbital and auricular points) or if not available i.e. prone position, 5–7 external fiducial markers were applied to the scalp for registration. Preoperative MRI scans were obtained using a 1.5 or 3.0 T MRI scanner (MAGNETOM Sonata Maestro Class and MAGNETOM Trio, Siemens Healthcare, Erlangen, Germany). Continuous T1WI and T2WI with 2-mm slices scans were performed for all the patients. Additionally, 3D T2 coronal fluid-attenuated inversion recovery (FLAIR) sequences with 1-mm slices was done when the margin of epileptogenic zone was unclear; 3D T1 enhanced sequences was performed for tumor-like lesion. The acquired

images were transferred onto the workstation, 3D model of the patients was reconstructed. After general anesthesia, the patient's head was placed in a Mayfield three-point head fixation system, the dynamic reference frame was attached to the clamp, the anatomic or scalp fiducials were used for registration. The navigation system then estimated the accuracy of the mathematical match between the scan and physical space. If the error was larger than 2 mm, registration and calibration should be carried out again.

2.3. Surgical technique

The neuronavigation system was incorporated for planning an ideal incision and approach according to the positions and the relationships between the lesion or targets, and the surrounding cerebral structures. A sterile dynamic reference frame was replaced, and maintenance of registration accuracy was confirmed. Microsurgical techniques were used with the aid of intraoperative neuronavigation in checking the match of planned approach and the real-time viewing field of the microscope. Resection or disconnection was executed completely based on the requirements of each type of surgery.

2.4. Follow-up

Patients were followed-up at 3, 6, and 12 months postoperatively by outpatient visits, then annual follow-up was performed by outpatient visits or telephone interview. Postoperative seizure outcome at the last visit was evaluated using Engel classification [19]. Demographic information and clinical presentations of epilepsy, type of surgery and seizure outcome according to Engel classification were collected for analysis.

3. Results

Totally 173 patients with medically refractory epilepsy who were treated surgically with the assistance of neuronavigation were included, male was slightly dominated (56.06%). Mean age at onset and receiving surgery were 17.35 ± 16.11 and 24.63 ± 15.61 years old, respectively. The range of age was large since we included both adult and pediatric patients. One hundred and four patients underwent resection of epileptic zone, that was the major surgery type with 60.12%. Within these patients, cerebral cavernous malformations ($n = 34$, 32.69%) and focal cortical dysplasia ($n = 33$, 31.73%) were the most common. Overall the mean follow-up period was 71.88 ± 42.86 months. An excellent seizure outcome, Engel Class I was found in 50.86% of the patients, followed by 23.12% patients with a good outcome of Engel Class II (Table 1).

Table 2 presented the outcomes of the patients, stratified by types of surgery. More than half of patients in each surgical type could achieve Engel Class I outcome, except for patients who underwent anterior subtotal callosal section. Only 25.71% had Engel Class I outcome, the majority were 31.43% with Class II and 28.57% with Class III in patients underwent anterior subtotal callosal section.

Contralateral visual field defect was found in all patients who underwent TPO disconnection. Other complications in patients who underwent TPO disconnection were followings: two (8.7%) patients had cerebral edema and one needed craniotomy to remove the swelling tissue. One patient had incision infection, surgical debridement was required. Disconnection syndromes were found in 18 (51.42%) patients who underwent anterior subtotal callosal section, all of them were resolved within 3 weeks. Among patients underwent functional hemispherectomy, 7 (63.64%) patients had decreased muscle strength in contralateral extremities and 5 patients recovered to the preoperative levels within 6 months. Two patients still had decreased muscle strength in the upper extremities. Decreased muscle strength in the left upper extremities was found in one patient who underwent resection of epileptic zone. One patient with cerebral cavernous malformations had

Table 1
Demographic data of 173 patients with refractory epilepsy.

	Number of patients (%)
Gender	
Male	97(56.06)
Age of onset [year, mean ± SD (range)]	17.35 ± 16.11(0.1–59)
Age of receiving surgery [year, mean ± SD (range)]	24.63 ± 15.61(1.8–61)
Duration of epilepsy [year, mean ± SD (range)]	7.27 ± 6.88(0.4–36)
Type of surgery	
Temporo-parietal-occipital disconnection	23(13.29)
Anterior subtotal callosal section	35(20.23)
Functional hemispherectomy	11 (6.36)
Resection of epileptic zone	104(60.12)
Type of epileptic zone	
Focal cortical dysplasia	33(31.73)
Tuberous sclerosis complex	3(2.88)
Gray matter heterotopia	5(4.8)
Neoplasm	29(27.88)
Cerebral cavernous malformations	34(32.69)
Follow-up period [Month, mean ± SD (range)]	71.88 ± 42.86(12–169)
Engel epilepsy surgery outcome	
Class I	88(50.86)
Class II	40 (23.12)
Class III	34(19.65)
Class IV	11(6.36)

incision infection and recovered after oral administration of antibiotics.

4. Discussion

In this study, we retrospectively reviewed the surgical outcome of using neuronavigation to assist 4 types of surgery for treating medically refractory epilepsy in our hospital across almost 10 years. Overall around half of the patients (50.86%) achieved excellent seizure outcome of Engel Class I, complications were manageable. These results indicated that the applicability of neuronavigation, and the use of neuronavigation provides good efficacy and safety for all kinds of surgical procedures for patients with medically refractory epilepsy.

Accurate positioning is required both for preoperative planning and intraoperative process of epilepsy surgery. Neuronavigation can easily combine several imaging modalities, including CT, MRI or angiographic scans into one data set, and provide visible spatial relationships with the invisible part of brain to the naked eyes [20]. A comprehensive systematic review indicated that comparing to conventional epilepsy surgery, the performance of surgery with neuronavigation is merely equivalent in its efficacy and safety, however, the need for resection and rate of neurological deficits is reduced [21]. We compared our results to the first randomized, controlled trial of surgery for temporal-lobe epilepsy which was believed neuronavigation was not used [8], the results may indicate the same conclusion, 58% patients in surgery group (n = 40) were free of seizures impairing awareness at one year in the trial, which is closed to our results, 50.86% (n = 88) had Engel class I epilepsy surgery outcome. Moreover, this trial included temporal lobe epilepsy only, the epileptogenic lesion(s) of temporal lobe usually could be successfully resected without the assistance of neuronavigation, because of the low risk due to more clearly anatomic structures and

Table 2
Engel epilepsy surgery outcome stratified by type of surgery.

Type of surgery	Number of patients, total	Engel epilepsy surgery outcome [Number of patients (%)]			
		Class I	Class II	Class III	Class IV
Temporo-parietal-occipital disconnection	23	12(52.17)	5(21.74)	4(17.39)	2(8.7)
Anterior subtotal callosal section	35	9(25.71)	11(31.43)	10(28.57)	5(14.29)
Functional hemispherectomy	11	9(81.82)	1(9.09)	1(9.09)	0(0)
Resection of epileptic zone	104	58(55.77)	23(22.12)	19(18.27)	4(3.85)

more reachable locations. In our experience and some studies, on the other hand, the application of neuronavigation in neurosurgery remained beneficial. The trial only included temporal-lobe surgery, our study included total 4 types of procedures with advanced difficulty. In addition, a systematic review of 32 studies involving 2250 patients in 2003 examined the efficacy in seizure control of conventional neurosurgery for epilepsy, the results found that only 65% patients had seizure control, indicated the improvement cause by using neuronavigation [3]. For the reason that it provides the surgeons more confidence, and reduces the incidence of incision infection and the lengths of both operation and hospital stay [20,22], possibly as a result of the reduced resection volume and the subsequently reduced postoperative complications.

The major challenge of neuronavigation is brain shift, which is the representation of movements or dislocation of the brain parenchyma between preoperative images and intraoperative brain anatomy [20,23], due to the loss of cerebrospinal fluid or resection of brain tissue, cyst decompression, cerebral edema during surgery. Different strategies could be applied to overcome the challenges for different surgical types. When TPO disconnection was performed, since the level of brain shift of the lateral ventricles near the middle line is lower than other parts, we used periinsular approach into the lateral ventricles, then disconnection of white matter tracts was conducted via the intraoperative guidance of neuronavigation to determine the angle and depth. Vessel features and falx cerebri of the 3D reconstruction can be used as landmarks to correct the brain shift intraoperatively. According to the same principle as correction of brain shift during TPO disconnection, combination of neuronavigation to identify the genu and splenium of corpus callosum and to determine the angle of dissection of frontal lobe tract, functional hemispherectomy can be performed without injuring thalamus or incomplete dissection. For patients underwent resection of epileptic zone, intraoperative MRI was required to update the registration and maintain the accuracy of neuronavigation. The placement of depth electrodes for EEG monitoring during surgery was guided by neuronavigation, aiming to achieve complete resection of epileptic zone. For anterior subtotal callosal section, the level of brain shift is small after loss of cerebrospinal fluid, we can directly identify the splenium to dissect subtotal corpus callosum by neuronavigation.

Providing better spatial orientation is the advantage of neuronavigation. This is more important for patients who need functional hemispherectomy, since usually they also featured anatomical deformity, such as hemimegalencephaly, that accurately positioning by anatomical markers become difficult, therefore, lead to incomplete disconnection and increase resection rate [24]. Enhanced orientation during surgery can decrease the resection volume and avoid resection of eloquent regions during anterior subtotal callosal section. The shape of corpus callosum may lead to inaccurate estimation of the depth and width of resection based on preoperative imaging only, intraoperative neuronavigation guidance helps much during the surgery [16]. The Engel epilepsy surgery outcome for patients underwent anterior subtotal callosal section were not as good as patients who were treated by other types of surgery. In addition to the complexity of the procedure, the criteria of patient selection is probably more important since drop attack is the primary criteria for anterior subtotal callosal section, which

is the most severe seizure type, and limited the improvement of seizure outcome postoperatively. A smaller incision can be designed by neuronavigation for TPO disconnection to reduce the blood loss and tissue injury, only the essential part, postcentral region from 2.5 cm to the midline, down to the posterior temporal operculum was exposed [15].

Several limitations in this study should be mentioned. As a retrospective, single-hospital study, there was no control group for comparison to clearly demonstrate the benefit of using neuronavigation. Surgical and clinical trials could be conducted with appropriate research designs.

In conclusion, in our retrospective study, we reported our single-hospital experience of neuronavigation-assisted surgical treatments for medically refractory epilepsy. In 4 types of surgeries, TPO disconnection, anterior subtotal callosal section, functional hemispherectomy and resection of epileptic zone, more than 70% of patients achieved Engel I and II epilepsy surgery outcome. Surgical intervention could be considered and encouraged for patients with medically refractory epilepsy because of the efficacy and safety.

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Conflict of interest

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval

This is a retrospective study, for this type of study formal consent is not required.

Informed consent

This article does not contain any studies with human participants performed by any of the authors.

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