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Hippocampal deep brain stimulation in nonlesional refractory mesial temporal lobe epilepsy

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ABSTRACT

Purpose: To evaluate the efficacy of chronic continuous hippocampal deep brain stimulation (DBS) in nonlesional refractory mesial temporal lobe epilepsy.
Methods: Three adult patients with medically intractable epilepsy treated with hippocampal DBS were studied. Two patients underwent invasive recordings with depth stereo-electroencephalography (SEEG) electrodes to localize ictal onset zone prior to implantation of DBS electrodes. All the patients with no lesion in brain magnetic resonance imaging (MRI) scan received bilateral implantation of DBS electrodes. Chronic continuous high-frequency hippocampal stimulation was applied during treatment. The number of seizures in each patient before and after stimulation was compared.
Results: Long-term hippocampal stimulation produced a median reduction in seizure frequency of 93%. Two out of these patients received unilateral activation of the electrodes and experienced a 95% and 92% reduction in seizure frequency after hippocampal DBS respectively. The last patient had bilateral electrode activation and had a seizure-frequency reduction of 91%. None of the patients had neuropsychological deterioration and showed side effects. Generalized tonic–clonic seizures disappeared completely after hippocampal DBS.
Conclusions: Chronic continuous hippocampal DBS demonstrated a potential efficiency and safety in nonlesional refractory mesial temporal lobe epilepsy and might represent an effective therapeutic option for these patients.

1. Introduction

Epilepsy is one of the most common neurological diseases which affects 0.5–1% of the general population [1]. Despite formal anti-epileptic drugs treatment, up to 30% of patients still have uncontrolled seizures [2,3]. Mesial temporal lobe epilepsy is a particularly frequent common form of medically intractable epilepsy [4]. Nonlesional refractory mesial temporal lobe epilepsy characterized by epileptiform discharges in one side or both sides temporal lobes and normal brain MRI scan is not good candidate for ablative surgery of selective amygdalo-hippocampal complex alone or together with the anterior temporal lobe [5–8]. For these patients, hippocampal DBS has been proposed as a potential therapeutic option.

We present the results obtained from these patients with nonlesional refractory temporal lobe epilepsy who underwent hippocampal DBS.

2. Material and methods

2.1. Patients

Three adult patients with intractable temporal lobe epilepsy were treated with bilateral DBS electrodes implantation at Department of Functional Neurosurgery of Hebei General Hospital between June 2010 and December 2013. The presurgical evaluation included 3T brain MRI, video-EEG telemetry, interictal positron emission tomography (PET), SEEG, magnetoencephalogram as well as neuropsychological and psychiatric assessments.

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Table 1
Demographic characteristic of neuroimaging, invasive video-EEG recording, AED, and etiology.

Pt	MRI	Type	AED(md/d) Pre-DBS	Ictal onset	Etiology
1	Normal	CPS	OXC 900, VPA 1000	L focal MT	Birth injury
2	Normal	CPS	VPA 1000, CBZ600, LEV 1000	L focal MT	Craniocerebral injury
3	Normal	CPS + GTCS	VPA 1000, LTG200	R regional MT with early Left-sided involvement	Febrile convulsion

Pt: patient number; LGT: lamotrigine; LEV: levetiracetam; VPA: valproicacid; OXC: oxcarbazepine; CBZ: carbamazepine; CPS: complex partial seizure; GTCS: Generalized tonic–clonic seizure; MT: mesial temporal.

The following clinical symptom characteristics were considered diagnostic for temporal lobe epilepsy: ascending epigastric aura or fear followed by complex partial seizures (CPS) characterized by staring and oropharyngeal automatisms (smacking lips, masticating) which may be accompanied by ipsilateral superior limb automatisms or contralateral superior limb dystonia, possibly progressing late to generalized tonic–clonic activity. The cause of epilepsy was not yet clear, which might be associated with birth injury, craniocerebral injury and febrile convulsion (Table 1).

Two patients underwent stereotactic depth electrodes implantation for intracranial invasive monitoring to localize ictal onset zone before DBS electrodes implantation because of insufficient proof on scalp video-EEG recordings. Multiple contact intracerebral electrodes (diameter, 0.8 mm; 5–18 contacts, 1.5 mm in length and 2 mm apart [Dixi Medical, Besançon, France]) were implanted. A high resolution CT scan was performed after implantation of the SEEG electrodes to evaluate lesions and co-registered with the preoperative 3D T1-weighted MRI to allow precise localization of the electrode contacts. It took ten days from removal of the depth recording electrodes to implantation of DBS electrodes.

These entry standards included: (1) seizure frequency of at least one complex partial seizure per month, (2) epileptic discharges in temporal lobes due to scalp video-EEG recording, (3) ictal onset zone located in unilateral temporal lobe owing to invasive video-EEG monitoring and (4) no lesion in MRI scan.

All candidates understood the operational risks and curative effects fully, signed their operation informed consents in this study conducted by the Ethics Committee of Hebei Medical University.

2.2. Implantation procedure of DBS electrodes and stimulation paradigm

A computerized tomography scan acquired under stereotaxic head frame (CRW, Radionics, USA) was fused with the 3D T1-weighted MRI. A plan was made based on stereotactic CT/MRI fusion. The permanent quadripolar DBS electrodes (Medtronic 3487A) were inserted into the bilateral hippocampal heads perpendicular to the hippocampal longitudinal axis through frontal burr holes under general anesthesia. The third and fourth contacts were located in hippocampal head on each side as determined by the fused CT/MRI datasets, while the first and second contacts were located in parahippocampal gyrus (Fig. 1). Intra-operative neuronavigation was used during electrode insertion. Each electrode has four cylindrical contacts. The electrodes were connected to the ipsilateral pulse generators (Medtronic Soletra 7426) implanted in subclavicular pockets through the subcutaneous wires (Fig. 2).

Chronic continuous high frequency stimulation was employed during treatment. The pulse width was set to 450 μs and remained unchanged in the whole course of treatment. The quadripolar configuration of DBS was employed in which the first contact was set as cathode and the fourth contact was set as the anode.

The stimulating frequencies of 130, 150 and 170 Hz were suggested in patients 1, 2, and 3 respectively.

The voltage was increased gradually by 0.1 V every 2 months if the DBS failed to decrease seizures by ≥90%, to a highest at 3.5 V, or until the patients became seizure-free or adverse reactions appeared.

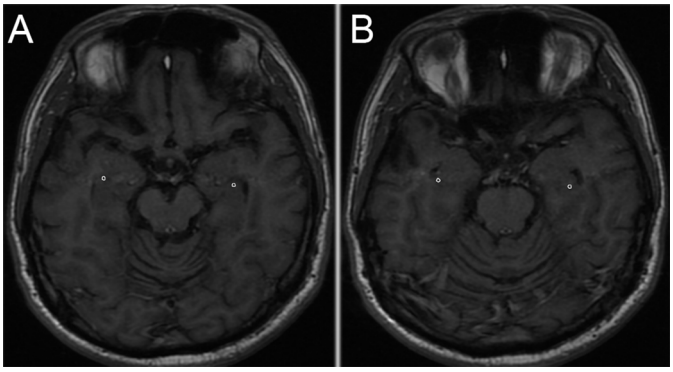

Fig. 1. Position of the DBS electrode contacts in bilateral hippocampal heads. The images after fusion of postoperative CT and preoperative MRI revealed that the bilateral white round rings were intracranial DBS electrodes in bilateral hippocampal heads. The third and fourth contacts were located in hippocampal head on each side, while the first and second contacts were located in parahippocampal gyrus. (A) the fourth pair of DBS electrode contacts and (B) the third pair of DBS electrode contacts.

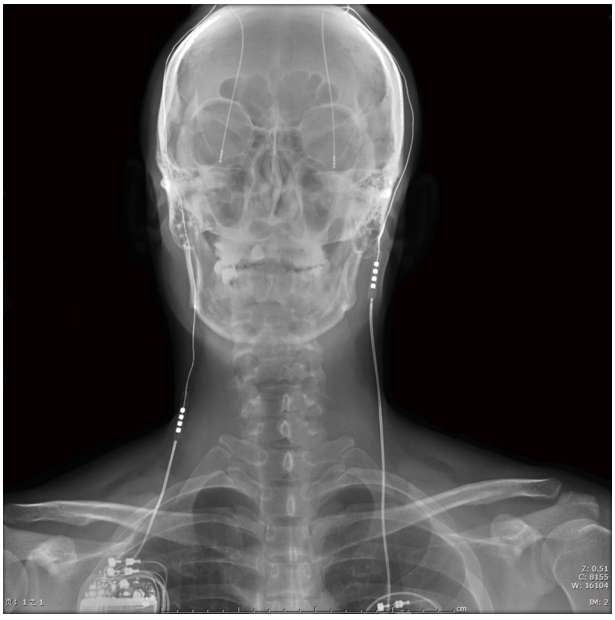

Fig. 2. Intracranial stimulus devices. The photos showed the intracranial stimulus devices including the bilateral depth electrodes inserted into the hippocampal heads through frontal burr holes and the bilateral subcutaneous wires connected the electrodes and the pulse generators.