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Long-term follow-up of anterior thalamic deep brain stimulation in epilepsy: A 11-year, single center experience

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ABSTRACT

Purpose: Anterior thalamic deep brain stimulation (ATN DBS) is an emerging, effective treatment for patients with drug-resistant epilepsy, but long-term results on its efficacy and safety are lacking. To evaluate the long-term efficacy and safety of ATN DBS treatment, as well as predictors of its success, in patients with drug-refractory epilepsy (DRE).
Method: We retrospectively studied clinical outcomes in 29 consecutive refractory epilepsy patients treated by a single DBS team (two neurosurgeons, four neurologists) over an 11-year period, for whom follow-up was performed for up to 137 months (mean, 74.9 months).
Results: The average participant was 30.7 (±10.4) years old and had epilepsy for 19.3 (±9.0) years. The mean preoperative frequency of disabling partial or generalized tonic-clonic seizures was 27.5 (±8.6, SE) seizures a month. The median percent seizure reduction was 71.3% at 1 year, 73.9% at 2 years, and ranged from 61.8% to 80.0% over post-implant years 3 through 11 in the long-term study (overall 70% median reduction). In the 11-year study period, 13.8% (4/29) of subjects were seizure-free for at least 12 months during this time. There was only one symptomatic intracranial hemorrhage that happened during follow-up (3.4%). Infection requiring removal and later re-implantation of hardware occurred in only 1 of 30 patients (3.3%), who was subsequently excluded from our follow-up assessment. Hardware malfunction including lead disconnection occurred in 2 of 29 cases (6.9%). Revision of lead position to redeem poor clinical response was performed in 3 of 58 implanted leads (5.2%).
Conclusions: ATN DBS can be an effective therapy in a variety of patients with DRE. Importantly, we provide evidence that significant therapeutic efficacy can be sustained for up to 11 years. Neurological complications were rather rare, but long-term hardware-related complications should be followed arrectis auribus.

1. Introduction

Despite the introduction of modern anti-epileptic drugs (AED), approximately 30% of patients continue to have refractory seizures that adversely affect their quality of life [1,2]. Electric modulation of epileptic neural circuits via an implanted neuro-stimulator system, including deep brain stimulation (DBS), has been recognized as a promising alternative therapeutic choice for patients with epilepsy [3–6]. Among various neural targets for DBS, the anterior nucleus of the thalamus (ATN) is a central node in the Papez circuit [7]. It receives input from the mesial temporal areas via the fornix, and has efferent connections to the ipsilateral cingulate, antero-mesial frontal and temporal lobes [8]. Although the mechanistic underpinnings of the anti-seizure efficacy of DBS remain unclear, modulation of the ATN with DBS is an attractive option for patients with drug-refractory epilepsy (DRE).

Long-term follow-up data for epilepsy patients treated with DBS is scarce. Very recently, long-term efficacy and safety data from the SANTE trial (Stimulation of the Anterior Nucleus of the

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Thalamus for Epilepsy) was released, with this stimulation treatment showing sustained efficacy and safety in a treatment-resistant population [9]. In the present study, we report a retrospective analysis of seizure outcomes conducted to analyze the efficacy and safety of ATN DBS for drug-refractory patients at our institution since the first implant was placed in 2005, and examine predictors of ATN DBS treatment success. In addition, we sought to investigate the long-term cognitive changes resulting from chronic ATN DBS.

2. Patients and methods

2.1. Study design

The data used in the present study were collected via retrospective review of the medical records of 30 consecutive patients with DRE who were treated with ATN DBS by our neuromodulation team. DBS surgery was administered to these patients by two neurosurgeons (KJ Lee and BC Son) and four neurologists (SH Kim, SC Lim, J Kim and YM Shon) at 2 Catholic University Hospitals (Yeouido St. Mary's and Seoul St. Mary's Hospital) over an 11-year period [10–12].

2.2. Patients

Our criteria for bilateral ATN DBS implantation have been published previously [12]: frequent (>4 per month) and disabling seizures not controlled by multiple AED treatment modalities; not a candidate for resective surgical treatment as determined by video-EEG monitoring (e.g. multifocal ictal onset zone); previously failed resective or disconnection surgery; patients (or caregivers) agreed to keep a daily seizure diary for a 3-month baseline period before DBS implantation and continuously after initiation of treatment; patients (or caregivers) agreed that no changes to the baseline presurgical medication regimen would be made during at least the first year after DBS implantation. The study was conducted with the approval of the Institutional Review Board (SC11OISI0013) of the Catholic University of Korea, and informed written consent was obtained from all patients or from their family members.

Thirty consecutive patients who underwent ATN DBS treatment for DRE between 2005 and 2015, and who had follow-up evaluations for more than 1 year, were included. Follow-up evaluations were conducted during routine outpatient clinic visits, hospital visits for reoperation or scheduled battery changes, and via phone interviews.

2.3. Surgical technique and programming of device

Each patient underwent frame-based, microelectrode-guided, stereotactic implantation of DBS leads (model 3389 or 3387; Medtronic® Inc., Minneapolis, Minnesota, USA). The cost of the surgeries were mostly reimbursed by Korean national healthcare insurance. ATN implantation was performed with either local or general anesthesia using a Leksell frame. We targeted the ATN on the parasagittal magnetic resonance imaging (MRI) as a prominence in the inferior wall of the lateral ventricle. The insertion of DBS electrodes (model 3387 or 3389; Medtronic® Inc.) and implantable pulse generators (IPGs, model Soletra or Activa SC; Medtronic® Inc.) was performed as previously described [10,13]. We confirmed electrode placement within the ATN with postoperative imaging – either brain CT (21 patients) or MRI (9 patients). Activation and programming of the IPGs started 1 or 2 weeks after implantation. The initial parameters were similar to the parameters used for surgery for movement disorders (high frequency of 130 Hz; pulse width of 90 microseconds; continuous stimulation). Using a previously reported programming algorithm [12], the relatively low voltage (1.5 ~ 3.1 V) stimulation and monopolar configuration were adjusted on the basis of improvement in seizure frequency and minimizing side effects.

2.4. Variables to be assessed

Long-term follow-up and adjustment of DBS parameters were conducted by the authors (YM Shon, SH Kim and J Kim). Retrospective chart review was performed to collect follow-up

Table 1
Demographic data.

Characteristics of patients (total 29 pts)	No (%) or mean ± SD (range)
Age (y)	30.7 ± 10.4
Female sex	10 (34.5%)
Age at seizure onset	11.9 ± 8.6
Duration of epilepsy prior to DBS	19.3 ± 9.0
Age at DBS insertion	29.0 ± 16.5 (1.3–76)
Mean follow-up (y)	6.0 ± 3.2
Mean seizure frequency (/M)	65.7 ± 221.6
Median seizure frequency (/M)	10 (4–1200)
Type of Seizures (diabled, n)	
Complex partial	28 (96.6%)
focal motor	5 (17.2%)
Primary generalized	1 (3.4%)
Symptomatic generalized	4 (13.8%)
Drop attack	3 (10.3%)
Myoclonic	2 (6.9%)
Secondary generalized	20 (69.0%)
Epilepsy Diagnosis	
Temporal lobe epilepsy with bilateral ictal onset	9 (31.0%)
Frontal lobe epilepsy or frontal dominant neocortical onset	8 (27.6%)
Multifocal epilepsy with extrafrontal dominant ictal onset	11 (37.9%)
Lennox-Gastaut syndrome	1 (3.4%)
Number of AEDs	4.3 ± 2.7 (2–8)
Number of AEDs failed	5.2 ± 4.1 (2–10)
Prior failed intracranial epilepsy surgery	6 (20.7%)
Number of seizure types	2.3 ± 0.6 (1–4)
Developmental delay	9 (31.0%)