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Original research article

Intracerebral electroencephalography in targeting anterior thalamic nucleus for deep brain stimulation in refractory epilepsy

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A B S T R A C T

Background: Results of DBS of ATN in refractory epilepsy depend on accuracy of the electrode's location. We searched for characteristic intraoperative, intracerebral EEG recording pattern from anterior thalamic nuclei (ATNs) as a biological marker for verifying the electrode's position.

Methods: There were six patients with refractory epilepsy scheduled for deep brain stimulation (DBS) procedure. At surgery, to map the target, we recorded EEG from each lead of DBS electrodes. One patient underwent a 24 hours EEG with continuous recording from both ATNs before internalization of stimulator units.

Results: In all patients we recorded spontaneous bioelectric activity of ATNs. The pattern of the recording from the ATN was similar in all cases. In the one patient where 24-hour recording was done with simultaneous scalp EEG, a complex partial seizure was captured.

Conclusion: This is the first report of using DBS electrode for intraoperative EEG recordings from the ATN in patients with refractory epilepsy. Since we managed to find the characteristic pattern of bioelectric activity of ATN, this technique seems to be a promising method for targeting this structure during the operation.

1. Introduction

Since its introduction deep brain stimulation (DBS) has been successfully used in movement disorders [1] and in neuropsychiatry [2]. Essentially, DBS inhibits pathologic network activity of a chosen brain region in a reversible way without damaging brain tissue [3]. Thus, although it provides no cure, it lessens the symptoms and improves quality of life. A list of DBS targets in refractory epilepsy includes cerebellum [4–6], subthalamic nucleus [7,8], hippocampus [9,10], basal ganglia and various thalamic nuclei [11,12], however, so far no optimal target suitable for the majority of the patients has been defined. In recent years, a controlled multicentre trial SANTE was published, showing very promising results of the bilateral ATN stimulation [13,14]. The candidates recruit out of those

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with refractory partial seizures, including secondarily generalised seizures, in whom the epileptic focus cannot be localised, or it is located in an eloquent brain area, or else if there are multiple epileptic foci. ATN stimulation was also used in patients after failed resective epilepsy surgery. Efficacy of the procedure primarily depends upon the choice of the target and precision of positioning the electrodes. However, all currently employed methods of localising the ATN are subject to bias. The aim of our study was to find the characteristic intraoperative, intracerebral EEG recording pattern from the ATN, which could be used as a biological marker for verifying accuracy of the electrode's position. Understandably, finding of such a marker could improve on precision of the electrode placement and efficacy of the stimulation which would translate into better operative results. Another goal was to assess the influence of the intraoperative high-frequency bipolar ANT stimulation on bioelectric activity of the both ATNs and of the cerebral cortex, the latter visible on the surface EEG recording.

2. Materials and methods

The study plan was approved by the Ethical Committee. All patients have given their informed consent for participation in the research study. There were six patients with refractory epilepsy scheduled for DBS procedure. Before surgery, in attempt to localise the ictal onset zone, we performed an MRI scanning and long-term video-EEG (LTM), which lasted 72 h. Clinical features of the patients are summarised in Table 1. In each patient the DBS electrodes (Medtronic model 3387 or 3389) were implanted streotactically (Stryker–Leibinger stereotactic frame) to both ATNs. The target and trajectory were chosen individually basing on typical MRI landmarks. Surgical plan was performed using Brainlab software. The surgical target was chosen 5–6 mm lateral, 12 mm superior and up to 2 mm anterior to midcomissural point (MCP). The target was verified taking into account individual anatomy of the mamillo-thalamic tract, which was considered as a landmark. The trajectory was planned to avoid major vascular structures seen in contrast enhanced T1-weighted MR images. All procedures were carried out under general anaesthesia – TIVA (total intravenous anaesthesia: midazolam 0.1–0.4 mg on induction and propofol 6–12 mg per 1 kg per hour along with fentanyl 0.05 mg/10 kg throughout the procedure). In every patient we recorded an intracerebral EEG (Grass Technologies, USA) directly from the DBS electrodes (separately from each lead for at least 30 min on each side) placed in the ATNs and simultaneously we performed a scalp EEG with gold-cup electrodes placed at points Fp1, Fp2, F7, F8, T3, T4, T5, T6, O1, O2 according to the international 10–20 system. The other surface EEG electrodes, which would have to be placed in the operating field, thus incommoding the surgeon, were not used. For the scalp EEG recording the conventional referential montage was used. The location of the leads in the ATN was confirmed by means of single-unit microelectrode recordings (MER) – (LeadPoint, Medtronic). Then, in all the patients we performed high-frequency bipolar stimulation of the ATN with the implanted DBS electrode (two adjacent contacts, 1–5 V, 90 μsek, 145 Hz; the stimulation pattern was: 2 cycles of 3 min on – 2 min off) whilst assessing influence of the stimulation on the recording from the ipsilateral and opposite ATN as well as on the scalp EEG. Moreover, before internalisation of the stimulator units and tunnelling the electrode and extension wires, one patients underwent a 24 h surface EEG monitoring with continuous intracerebral recording from both ATNs (taken from each lead of the implanted DBS electrodes). After surgery, the electrodes position was verified on the postoperative thin slice CT fused with the preoperative MR images [15].

The clinical results were assessed at 3 months intervals on follow-up out-patient clinic. The total follow-up period was from 18 to 24 months. Reduction of 40–50% in the frequency of the seizures was noted in all cases. The detailed dates were given in Table 2. However, side effects were also observed: depression in 3 cases and memory impairment in 5 patients.

3. Results

MER turned out to be useful and confirmed the correct position of the ATN electrodes in every case (Fig. 1). The intracerebral

Table 1 – Clinical data.

Patient	Sex	Age	Years with epilepsy	Previous epilepsy surgery	MRI	Seizure onset zone
1	F	59	43	Left temporal lobectomy, VNS	Left temporal lobe resected. A small hypointense lesion in the right leticular nucleus.	Multifocal
2	M	43	12	Anterior callosotomy	CVM in the left temporal lobe. Ischaemic changes in the right frontal lobe	Multifocal
3	M	51	45	–	A small hyperintensive lesion in the left hippocampus (a vascular malformation?), DVM in the right occipital lobe.	MTLE R
4	M	34	29	Left temporal lobectomy	Thickening of dura in the region of the operation for cerebral abscess.	Left fronto-temporal
5	F	38	14	–	Right temporal and occipital heterotopia	Multifocal
6	M	39	38	–	Normal	Bi temporal

CVM = cavernous venous malformation, DVM = developmental venous malformation, MTLE R = mesial temporal lobe epilepsy right side, VNS = vagal nerve stimulator.