Deep Brain Stimulation of Anterior Thalamic Nuclei for Intractable Epilepsy in Thailand: Case Report

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Neurostimulation can be an alternative treatment for medically intractable epilepsy, especially when the resective surgery could not be performed. The author reported a case of a 19-year-old, right-handed male patient who had a history of intractable epilepsy for 11 years after post viral encephalitis associated with status epilepticus. Following the failure of antiepileptic medications and then resective surgery, anterior thalamic deep brain stimulation (DBS) was performed. Indirect targeting of anterior thalamic nuclei could not be used because of asymmetric brain shift from prior multilobar resections. Direct targeting of anterior thalamic nuclei from MRI T1 sequence, Short Tau Inversion Recovery (STIR) sequence combined neurophysiological mapping by microelectrode recording were used as a technique for implantation of DBS electrodes. The stimulation was turned on with 145 Hz, pulse width 90 microseconds, 5 volts with cycling mode 1 minute “on” and 5 minutes “off”. The antiepileptic medications continued the same as pre-operative state. Sixty percent seizure reduction was achieved in 24 months after surgery. There were no side effects of DBS during the follow-up period.

Anterior thalamic DBS can be performed safely with satisfactory seizure outcomes. Direct targeting of anterior thalamic nuclei combination with microelectrode recording can be very helpful, especially when asymmetric basal ganglion structures were detected.

Keywords: Anterior thalamic DBS, Medically intractable epilepsy, Neurostimulation

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of hippocampus and mesial frontal tissue. Unfortunately, the recurrent seizures occurred after 6 months of surgery. His seizures occurred in clusters, averaging about 8 seizures per month with complex motor seizures and secondary generalized tonic clonic seizures. The persistent interictal spikes were recorded over left posterior temporoparietal region. The further resection on left dominant hemisphere was not recommended because the higher risks of postoperative neurological deficits, especially language function and the higher recurrent seizures rate from the history of post viral encephalitis with status epilepticus. His antiepileptic medications included gabapentin 1,800 mg per day, levetiracetam 3,000 mg per day and lamotrigine 400 mg per day. The neuromodulation techniques, including vagal nerve stimulation and deep brain stimulation, can be the alternative surgical options to improve the seizure control and quality of life. Informed consent for surgery was obtained after all risks and benefits of deep brain stimulation for epilepsy control were explained.

Pre-operative evaluations included scalp EEG, volumetric 3T-MRI (Phillips) (T1 with gadolinium and STIR sequence) and neuropsychological tests. The targeting anterior nucleus of thalamic (ANT) was performed by stealth station (S7, Medtronic) few days prior surgical date. The combination of direct targeting and indirect targeting of ANT were applied. The transventricular trajectory was planned with respect to important vascular structures such as choroid plexus, thalamostriate veins. The patient underwent Cosman-Roberts-Wells (CRW) stereotactic frame placement under local anesthesia in the morning of the operative date. Volumetric axial CT brain with contrast was done and fused with pre-operative MRI data. Then, the patient was intubated and microelectrode records were performed under general anesthesia. The surgery began on the left side, in which the ventricle is normally larger and ANT is smaller than the right side. The top of ANT was defined by the pattern changes from silent ventricular area into thalamic neuronal activities. The depth of electrodes was targeted about 7 mm from the top of thalamus and confirmed by lateral fluoroscopy. The procedures were the same on the right side, although the activities of neuron seem to be more robust than the left side (Fig. 1). The neurostimulator (Medtronic, kinetra) was connected to the DBS leads (Medtronic, 3389) after removal of the frame. The patient was doing well after surgery and discharged on the third-day post-operative. The post-operative CT brain (on the second day) revealed minimal pneumocephalus without postoperative bleeding. The postoperative MRI brain T1 revealed good electrodes’ positions in the bilateral ANT (Fig. 2). The patient initially was followed-up every 2 weeks during stimulation adjustment starting from 3 volts, frequency at 145 Hz, pulse width 90 microseconds with cycling mode 1 minute “on” and 5 minutes “off” and gradually increased to 5 volts. His seizure was improved overall with 60 percent reduction in frequency and duration during a two-year follow-up period. Only few secondary generalized tonic-clonic seizures were reported, when battery accidentally shut off itself. No other side effects were reported.

**Discussion**

Data from animal epilepsy models of anterior nucleus of thalamus stimulation in seizure control were reviewed and demonstrated the effectiveness to control epilepsy\(^{(5-7)}\). The SANTE trial outcomes and other retrospective data reassured the effectiveness of ANT stimulation as an option for improving seizure control and quality of life of these medically intractable epilepsy patients\(^{(2)}\). Indications of surgery for these patients are: firstly, the refractory epileptic patient with disabling seizures, which affect quality of life; secondly, the epileptogenic zone cannot be safely treated by resective procedures; and lastly, the patient passes the neuropsychological evaluation.
The anterior nucleus of thalamus (ANT) is part of the circuit of Papez. This nucleus locates at the most rostral part of thalamus which is also called anterior tubercle. Its complex anatomy of this nucleus is divided into 3 parts known as anteroventral (AV, large principle nucleus), anteromedial (AM) and anterodorsal (AD)\(^8\). The large principle nucleus is about 4x5x10 mm\(^3\) in dimension. The input of ANT mainly arises from hippocampus, fornix and mammillothalamic tract, respectively. The output of ANT goes to cingulate gyrus and paralimbic structures to complete the circuit of Papez. The boundary of ANT is also important for direct targeting this small nucleus. The ventricular system serves as the border anteriorly and superiorly. The mammillothalamic tract connects into this nucleus inferiorly in coronal and sagittal plane. The lateral boundary separates from other thalamic nucleus by internal laminae.

Imaging sequence of ANT complex can be visualized from both MRI T1 and STIR. The STIR seems to increase the contrast between grey and white matter better than T2 sequence. The most important anatomical landmark for defining ANT is the identification of mammillothalamic tract, which can be followed as a dark signal from mammillary body to ANT. The mammillothalamic tract can be easily seen in coronal and sagittal view during the planning\(^9\). Targeting the ANT can be done indirectly from brain atlas by locating the midcommissural point (MCP) (Antero-posterior 0-2mm anterior to MCP, Lateral 5-6 mm from MCP and Vertical 12 mm superior to MCP). However, our case is a good example of brain asymmetry from previous surgery. The smaller left anterior thalamic nuclei can be observed on volumetric MRI, which most likely caused by wallerian degeneration from previous surgery. The indirect stereotactic coordinates put the target in the ventricular system at 12 mm above MCP. The final target of the left side is 8 mm above MCP, which is better visualized by direct targeting of ANT. The transventricular trajectory can cause some brain shift after CSF leakage, despite prevention with fibrin glue during assembling of the targeting device. This is the reason why the left side is being targeted first, except for the smaller nucleus as compared to the right side. Additional findings included the more robust neuronal activities on microelectrode recording in the right side, which corresponded to pre-operative MRI anatomical data. Even though, the neuronal signal of ANT may not be different from other thalamic nuclei, unlike subthalamic nucleus targeting. The neurophysiological target with microelectrode helps defining the top of ANT and possible the 4 mm thickness of this nucleus. The benefit of microelectrode recording is controversial in various centers\(^9\). The disadvantages of microelectrode recording included the risks of vascular injury with the sharp tip of electrodes, which can be avoided by pre-operative trajectory planning. Furthermore, the outcome correlation of electrode position was recently reported for good responder targets. Direct targeting of ANT is essential for the precision and effectiveness of the epilepsy outcomes\(^10\).

In conclusion, the anterior thalamic DBS can be offered as a treatment option for intractable epilepsy. The safety and effectiveness were well reported in the literatures\(^11\-13\). The present study reported the first anterior thalamic DBS for intractable epilepsy in Thailand. Direct targeting of anterior thalamic nuclei combination with microelectrode recording can be very helpful, especially when asymmetric basal ganglion structures were detected.

What is already known on this topic?
The anterior thalamic DBS is a new technique for controlling loop of epileptic network. The treatment is emerging after clinical trial and will be an option for specific group of intractable epilepsy.

What this study adds?
The first case experienced in Thailand with the method of targeting small nuclei, especially when asymmetrical basal ganglion was detected.

Potential conflicts of interest
None.

References
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