Anterior Thalamic Stimulation

Deep brain stimulation of the anterior nucleus of the thalamus (ANT-DBS) is a novel and promising treatment method for patients with drug-resistant epilepsy.

Clinical efficacy

More than 70% of patients implanted with ANT-DBS benefit significantly from this method, i.e., they report seizure-reduction rates higher than 50%

The median percent seizure reduction from baseline at 1 year was 41%, and 69% at 5 years. The responder rate (≥50% reduction in seizure frequency) at 1 year was 43%, and 68% at 5 years. In the 5 years of follow-up, 16% of subjects were seizure-free for at least 6 months. There were no reported unanticipated adverse device effects or symptomatic intracranial hemorrhages. The Liverpool Seizure Severity Scale and 31-item Quality of Life in Epilepsy measure showed statistically significant improvement over baseline by 1 year and at 5 years ($p < 0.001$).

Long-term follow-up of ANT deep brain stimulation showed sustained efficacy and safety in a treatment-resistant population.

Classification of evidence: This long-term follow-up provides Class IV evidence that for patients with drug-resistant partial epilepsy, anterior thalamic stimulation is associated with a 69% reduction in seizure frequency and a 34% serious device-related adverse event rate at 5 years. [1)].

Adverse events

When focusing on the adverse events reported in a study of stimulation of the anterior nuclei of thalamus (SANTE study), the patients reported paresthesia (18% patients), pain in the implant side (10.9% patients), and infection at the implant site (9.1% patients) [2)]

Literature search

Sobstyl et al. performed a literature search regarding the clinical efficacy of ANT DBS. They discussed the surgical technique of the implantation of DBS electrodes with special attention paid to the targeting methods of the ANT. Moreover, they present in detail the clinical efficacy of ANT DBS, with a special emphasis on the stimulation parameters, a stimulation mode, and polarity. They also report all adverse events and present the current limitations of ANT DBS.

In general, the safety profile of DBS in intractable epilepsy patients is good, with a low rate of surgery, hardware-related, and stimulation-induced adverse events. No significant cognitive declines or worsening of depressive symptoms was noted. At long-term follow-up, the quality-of-life scores have improved. The limitations of ANT DBS studies include a limited number of patients treated and mostly open-label designs with only one double-blind, randomized multicenter trial. Most studies do not report the etiology of intractable epilepsy or they include nonhomogeneous groups of patients

affected by intractable epilepsy. There are no guidelines for setting initial stimulation parameters. All the variables mentioned may have a profound impact on the final outcome.

ANT DBS appears to be a safe and efficacious treatment, particularly in patients with refractory partial seizures (three-quarters of patients gained at least 50% seizure reduction after 5 years). ANT DBS reduces most effectively the seizures originating in the temporal and frontal lobes. The published results of ANT DBS highlight promise and hope for patients with intractable epilepsy [3].

A literature review discusses the rationale, mechanism of action, clinical efficacy, safety, and tolerability of ANT-DBS in drug-resistant epilepsy patients. A review using systematic methods of the available literature was performed using relevant databases including Medline, Embase, and the Cochrane Library pertaining to the different aspects ANT-DBS. ANT-DBS for drug-resistant epilepsy is a safe, effective and well-tolerated therapy, where a special emphasis must be given to monitoring and neuropsychological assessment of both depression and memory function. Three patterns of seizure control by ANT-DBS are recognized, of which a delayed stimulation effect may account for an improved long-term response rate. ANT-DBS remotely modulates neuronal network excitability through overriding pathological electrical activity, decrease neuronal cell loss, through immune response inhibition or modulation of neuronal energy metabolism. ANT-DBS is an efficacious treatment modality, even when curative procedures or lesser invasive neuromodulative techniques failed. When compared to VNS, ANT-DBS shows slightly superior treatment response, which urges for direct comparative trials. Based on the available evidence ANT-DBS and VNS therapies are currently both superior compared to non-invasive neuromodulation techniques such as t-VNS and rTMS. Additional in-vivo research is necessary in order to gain more insight into the mechanism of action of ANT-DBS in localization-related epilepsy which will allow for treatment optimization. Randomized clinical studies in search of the optimal target in well-defined epilepsy patient populations, will ultimately allow for optimal patient stratification when applying DBS for drug-resistant patients with epilepsy [4].

Case series

Bilateral ANT electrodes were implanted into 18 patients suffering from focal, pharmacoresistant epilepsy. Antiepileptic treatment was kept unchanged from three months prior to operation. The Liverpool seizure severity scale (LSSS) was used to measure the burden of epilepsy.

Results: There was no significant difference between the 2 groups at the end of the blinded period at 6 months. However, when considering all patients and comparing 6 months of stimulation with baseline, there was a significant, 22% reduction in the frequency of all seizures (P = 0.009). Four patients had ≥50% reduction in total seizure frequency and 5 patients ≥50% reduction in focal seizures after 6 months of stimulation. No increased effect over time was shown. LSSS at 6 months compared to baseline showed no significant difference between the 2 groups, but a small, significant reduction in LSSS was found when all patients had received stimulation for 6 months.

Conclusions: Our study supports results from earlier studies concerning DBS as a safe treatment option, with effects even in patients with severe, refractory epilepsy. However, our results are not as encouraging as those reported from many other, mainly unblinded, and open studies [5].

Case reports

A case of relapsing herpes simplex encephalitis (HSE) as a newly reported and potentially fatal stimulation-related adverse effect following stimulation of the anterior thalamic nucleus (ANT-DBS) accompanied by fever, confusion, and cognitive impairment in a 32-year-old epileptic patient with a history of herpes meningoencephalitis 31 years earlier. The T2-weighted/FLAIR high-signal intensity in the temporal lobe developed at a “distance” from the stimulation target. The positive polymerase chain reaction of herpes virus deoxyribonucleic acid in the cerebrospinal fluid confirmed the diagnosis. The condition improved partially on acyclovir and stimulation stopped. Seizures disappeared and then returned after few months. The unique case report presents a rationale for considering history of herpes encephalitis as a relative contraindication for ANT-DBS, and HSE relapse should be suspected in patients with post-stimulation fever and/or altered consciousness [6].

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