EUROPEAN JOURNAL OF PAEDIATRIC NEUROLOGY 21 (2017) 223–231

Official Journal of the European Paediatric Neurology Society

Original article

Intracranial stimulation for children with epilepsy

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Keywords:
Epilepsy
Intracerebral
Cortical stimulation
Deep brain stimulation
DBS
Neuromodulation
Thalamus

ABSTRACT

Objectives: To evaluate the efficacy of intracranial stimulation to treat refractory epilepsy in children.

Methods: This is a retrospective analysis of a pilot study on all 8 children who had intracranial electrical stimulation for the investigation and treatment of refractory epilepsy at King's College Hospital between 2014 and 2015. Five children (one with temporal lobe epilepsy and four with frontal lobe epilepsy) had subacute cortical stimulation (SCS) for a period of 20–161 h during intracranial video-telemetry. Efficacy of stimulation was evaluated by counting interictal discharges and seizures. Two children had thalamic deep brain stimulation (DBS) of the centromedian nucleus (one with idiopathic generalized epilepsy, one with presumed symptomatic generalized epilepsy), and one child on the anterior nucleus (right fronto-temporal epilepsy). The incidence of interictal discharges was evaluated visually and quantified automatically.

Results: Among the three children with DBS, two had >60% improvement in seizure frequency and severity and one had no improvement. Among the five children with SCS, four showed improvement in seizure frequency (>50%) and one chid did not show improvement. Procedures were well tolerated by children.

Conclusion: Cortical and thalamic stimulation appear to be effective and well tolerated in children with refractory epilepsy. SCS can be used to identify the focus and predict the

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http://dx.doi.org/10.1016/j.ejpn.2016.10.011

effects of resective surgery or chronic cortical stimulation. Further larger studies are necessary.

1. Introduction

Around 0.4% of children under the age of 16 have epilepsy[1] and approximately 35% are not satisfactorily controlled by medical treatment. Children with refractory epilepsy are very difficult to manage, they consume substantial health resources, often have major disabilities and social disadvantage, and have higher risk of death from accidental causes, status epilepticus or Sudden Unexpected Death in Epilepsy (SUDEP), reaching up to 1% per annum.[2] Resective surgery is only considered as a treatment option when the area causing seizures can be removed without causing unacceptable neurological or cognitive deficits. In some cases, resective surgery is not an option due to proximity to eloquent cortex, presence of multiple foci, bilateral or generalized epilepsy.

Neurostimulation is an alternative for refractory patients who are not candidates for resection.[3] This technique delivers electrical pulses to specific areas of the nervous tissue with the intention of reducing the number and/or the severity of seizures (neuromodulation). In contrast to resective procedures, the technique is adjustable and reversible.

1.1. *Deep brain stimulation*

The effects of deep brain stimulation (DBS) on pharmacoresistant epilepsy have been under scrutiny since the 1970s,[4] and several structures have been targeted throughout the years.[5] The efficacy of thalamic stimulation depends on the epilepsy type. Stimulation of the anterior nucleus has proved to be effective for focal epilepsy showing that 54% of patients had seizure reduction of at least 50% after a 2 year follow up (Stimulation of the Anterior Nucleus of Thalamus for Treatment of Refractory Epilepsy (SANTE) trial[6]). Other studies have showed that the centromedian nucleus stimulation appears to be effective in generalised epilepsies.[7–9]

A low number of minors have been recruited with DBS. Seven children between four and 15 year old were implanted in the centromedian nucleus of the thalamus[10]; two children in the anterior nucleus of the thalamus,[6,11] one in the hippocampus,[8] and one in the subthalamic nucleus.[11] Authors reported that skin erosion might be of particular concern in children under eight years of age as a result of the relatively large size of the pulse generator and leads, originally designed for an adult population.[12] Reports elsewhere in this edition suggest that these issues may not be insurmountable.

1.2. *Cortical stimulation*

Interest in cortical stimulation as a therapeutic mean to reduce seizure activity began when Lesser et al. reported that during functional cortical mapping for potential resective surgery, epileptiform discharges could be terminated by brief electrical stimulation of the focus point.[12] In 2006 a case was published where, for the first time, continuous cortical stimulation was applied to the motor cortex in one patient for the treatment of focal epilepsy.[13] Ictal origin was within a functional area of the primary motor cortex, and consequently resective surgery was contraindicated. Assessment of stimulation through various electrode pairs surrounding ictal onset identified the most effective set of stimulation parameters in reducing interictal discharges. The patient's seizure frequency improved significantly over time, and after 4 years it decreased from 20 to 30 daily events to just one every other day, with no evidence of tissue injury or other adverse effects.

Regarding cortical stimulation, several studies have shown that hippocampal stimulation could be a useful alternative to surgical resection.[14–18] Another randomized controlled trial has shown efficacy of responsive (closed loop) neurostimulation of different cortical structures.[19–21] Chronic cortical stimulation of the primary motor cortex has been reported in only seven adults to date.[13,22–24] A recent article reported that a 4-day period of cortical stimulation in a 6 year old child with frequent seizures from multiple foci over the lateral temporal cortex, became seizure-free for 2 years after subacute cortical stimulation.[25] We have found no other report on the efficacy of cortical stimulation for the treatment of epilepsy in children.

1.3. *King's College Hospital experience in neuromodulation in epileptic children*

In the present study we discuss our preliminary experience with neuromodulation in 8 children with epilepsy. Three patients underwent electrode implantation for chronic thalamic deep brain stimulation (DBS). Five patients had a short period of cortical electrical stimulation during intracranial recordings in the video telemetry unit (hereafter called subacute cortical stimulation or SCS) with the purpose of identifying the candidate regions for further surgical treatment. The main aim of SCS is to identify the epileptogenic cortex in order to optimize future chronic treatment (resection, thermocoagulation or chronic stimulation). Given the significant long-term effects of chronic childhood epilepsy on educational attainment, employment, marital status, and psychological health into adulthood, this study may offer the potential to significantly improve the long-term quality of life of children with refractory epilepsy.

2. Materials and methods

2.1. *Patients*

This is a retrospective analysis on all 8 children treated with cortical and thalamic electrical stimulation for the investigation and treatment of refractory epilepsy at King's College