



Cortical stimulation parameters for functional mapping



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ABSTRACT

Purpose: There is significant variation in how patients respond to cortical electrical stimulation. It has been hypothesized that individual demographic and pathologic factors, such as age, sex, disease duration, and MRI findings, may explain this discrepancy. The purpose of our study is to identify specific patient characteristics and their effect on cortical stimulation, and discover the extent of variation in behavioral responses that exists among patients with epilepsy.

Method: We retrospectively analyzed data from 92 patients with medically intractable epilepsy who had extra-operative cortical electrical stimulation. Mapping records were evaluated and information gathered about demographic data, as well as the thresholds of stimulation for motor, sensory, speech, and other responses; typical seizure behavior; and the induction of afterdischarges.

Results: Ninety-two patient cortical stimulation mapping reports were analyzed. The average of the minimum thresholds for motor response was $4.15 \text{ mA} \pm 2.67$. The average of the minimum thresholds for sensory response was $3.50 \text{ mA} \pm 2.15$. The average of the minimum thresholds for speech response was $4.48 \text{ mA} \pm 2.42$. The average of the minimum thresholds for afterdischarge was $4.33 \text{ mA} \pm 2.37$. Most striking were the degree of variability and wide range of thresholds seen between patients and within the different regions of the same patient.

Conclusion: Wide ranges of thresholds exist for the different responses between patients and within different regions of the same patient. With multivariate analysis in these series, no clinical or demographic factors predicted physiological response or afterdischarge threshold levels.

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1. Introduction

Cortical stimulation for functional brain mapping has become an important tool for neurosurgeons and neurologists in the treatment of perirolandic and dominant neocortical temporal lobe epilepsy. For those patients with medically intractable epilepsy, excision of the entire epileptogenic focus is essential for long-term, seizure-free outcomes [1,2]. The epileptogenic focus is defined as the discrete anatomic location that generates a seizure which can then spread to distant sites [2]. This presents a challenge for attempted resection due to anatomical proximity of the epileptogenic focus to functional brain, namely the motor and sensory cortex, and language areas. The purpose of cortical stimulation mapping is to identify these areas in order to create boundaries for

surgical resection, and the technique is considered the gold standard for brain mapping [2].

Since cortical mapping was first implemented, there have been a variety of approaches and parameters used without a determined set of standardized guidelines [3]. Additionally, it is well established that there is significant variation in how patients respond to electrical stimulation [4–7]. One patient may demonstrate motor, sensory, language responses, and/or electrographic afterdischarges at relatively low levels of stimulation, while another patient may require a larger stimulus to produce the same reaction. It has been hypothesized that individual factors, such as age, duration of disease, type of lesion, and other variables, may explain this discrepancy [6,7]. Several studies have been conducted to investigate the influence of these factors, but none have definitively resolved these questions.

In our study, we retrospectively analyzed cortical stimulation mapping data from 92 patients with medically intractable epilepsy. These patients had pre-surgical evaluation, subdural

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electrode placement, and subsequent monitoring with intracranial EEG and cortical mapping in the ICU. The purpose of our study is to identify specific patient characteristics and their effect on cortical stimulation, and discover the extent of variation in behavioral responses that exists among patients with epilepsy. It is our goal to identify standards for cortical stimulation that will allow for safer, more effective, and tailored mapping for each individual.

2. Material and methods

2.1. Study group

This is an IRB-approved retrospective analysis using a prospectively maintained institutional epilepsy surgery database. Our study population consisted of consecutive patients who underwent subdural electrode placement by a single surgeon and then underwent subsequent cortical electrical stimulation mapping. The cortical stimulation mapping was performed by one of three experienced neurologists at our institution. Additionally, all patients underwent prolonged invasive subdural cortical electrode video-EEG monitoring. Functional and epileptogenic areas were assessed in all patients by cortical electrical stimulation and intracranial EEG recordings. Data was collected from the charts of these patients and detailed mapping reports, regardless of whether the patient had a following resective surgery. Data from depth electrodes was excluded in our analysis. There were 187 total patients who underwent subdural electrode placement during this time period, and out of these, 92 had completed mapping reports with either intraoperative pictures or scout imaging scans, so that the location of each electrode could be confirmed and included in the analysis.

2.2. Pre-surgical evaluation

Each patient was initially evaluated by completing a comprehensive history and physical exam, including age of disease onset, seizure semiology, past surgeries, use of anti-epileptic medications, and other past treatments. Patients underwent video EEG monitoring as well as appropriate imaging. For most cases, imaging included a 1.5 T MRI, and if negative, a 3 T MRI for selected cases. Some cases required additional imaging such as PET, SPECT, and SISCOM. Patients also underwent intracarotid amobarbital procedure (WADA test). This information was used to determine the dominant cortex, and the best type of electrodes and location for implantation.

2.3. Implantation of subdural electrodes

All surgeries were performed at a single institution by a single surgeon (RWB). Electrodes used were either strip electrodes or grid configuration. These consisted of stainless steel disks, each separated by 1 cm. Clinical information such as seizure semiology, imaging, and EEG data as well as gross anatomic assessment of cortex structure were used to guide placement of electrodes. Post-operative imaging, either x-ray or CT superimposed onto the MRI, was performed to confirm placement of the electrode contacts.

2.4. Intracranial EEG monitoring and cortical stimulation mapping

Intracranial EEG monitoring was performed immediately afterward and continued an average for one week after electrode implantation. Focal electrical stimulation of the cortex was carried out to determine the location of sensory, motor, and language areas of the cortex. Stimulation was performed to paired electrode contacts on the subdural grids and strips. Stimulation utilized a GRASS S12 biphasic stimulator constant current unit with 2 s

trains, with 0.3 impulses, at 50 Hz and 1.5–14.5 mA. The duration was fixed at 2 s for all functions tested, as it was adequate for all modalities. Amplitudes were measured from zero to maximum and they were biphasic. Generally, stimulation intensity was increased by 1.0 mA until an electrical afterdischarge (AD) or behavioral response was observed. The electrical intensity reached for each electrode pair was recorded as well as the location of that pair. All behavioral responses were noted, including speech arrest, motor activity, sensory changes, other behaviors not including speech, sensation, or motor activity, having the experience of typical aura or seizure, and pain which is thought to be attributed to dural stimulation. With this information, stimulation mapping reports were generated for each patient where functional brain area borders were identified and superimposed onto MRI or CT images.

2.5. Surgical resection

83 (90.2%) patients underwent seizure focus resection. This involved a second craniotomy with removal of the electrodes and resection of the epileptogenic focus, which was guided by the mapping report information. Intraoperative electrocorticography was often performed before and after resection to further confirm removal of tissue involved in the epileptogenic focus. Once the tissue was removed, a sample was sent to pathology for tissue analysis.

2.6. Follow up

Seizure frequency and severity were recorded from the last office visit. These outcomes were assigned a score according to the Engel Seizure Outcome Grading Scale: Class I: free of disabling seizures; Class II: rare disabling seizures (“almost seizure free”) or seizure-free intervals of 3–6 months; Class III: worthwhile seizure reduction (more than 75%); and Class IV: no worthwhile improvement with seizure reduction less than 75% and also recorded for analysis. All patients had greater than 1 year follow up.

2.7. Analysis

All relevant demographic features pertaining to each case and cortical stimulation sessions were cataloged, including age at surgery, sex, duration of disease, laterality and lobe location of electrodes, pathology results, MRI findings, and Engel Score. The measurement data for each patient was determined with minimums, maximums, and means, and these were analyzed as a group and presented as mean \pm standard deviation. Data compilation was performed using Microsoft Excel 2010 (Microsoft, Redmond, Wash., USA) and additionally, SPSS Statistics (Version 22.0 Armond, NY: IBM Corp.) was used for data analysis. Descriptive statistics were used to report the baseline characteristics and outcome profiles of all patients, and a correlation analysis was performed to investigate the correlation between the variables explored and thresholds for stimulation, with a p -value < 0.05 as significant. We then used a paired sample T test to compare the means between our variables.

3. Results

3.1. Characteristics of patients and disease pathology

A total of 92 patient cortical stimulation mapping reports were analyzed. There were 49 (53.3%) males and 43 (46.7%) females with an age range of 5–63 years. Electrodes were placed on the left hemisphere in the majority of patients (60.9%) and there was a

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