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Comparison of bipolar versus monopolar extraoperative electrical cortical stimulation mapping in patients with focal epilepsy

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HIGHLIGHTS

- We compared bipolar and monopolar cortical stimulation (CS) for mapping of eloquent cortex in patients undergoing subdural recording for presurgical evaluation of pharmacoresistant epilepsy.
- Bipolar CS required less stimulus current to elicit a clinical sign, but produced more afterdischarges when compared to monopolar CS.
- Clinical signs identified are similar with in both CS procedures, although monopolar CS is less time consuming.

ABSTRACT

Objective: Extraoperative cortical stimulation (CS) for mapping of eloquent cortex in patients prior to epilepsy surgery is not standardized across centres. Two different techniques are in use, referred to as bipolar and monopolar CS. We compared the ability of bipolar versus monopolar CS to identify eloquent cortex and their safety profile in patients undergoing subdural EEG recordings.
Methods: Five patients undergoing intracranial EEG recordings and extraoperative CS. Systematic comparison of stimulus parameters, clinical signs and afterdischarges of bipolar versus monopolar CS.
Results: Bipolar CS requires less stimulation current but is more time consuming and more likely to produce afterdischarges when compared to monopolar CS. None of the stimulations elicited seizures. The area defined as eloquent by either bipolar or monopolar CS reveals only minor discordances, involving mainly the outer row and edge of the electrode array producing clinical signs with monopolar CS only. Qualitatively, bi- and monopolar CS reproduced similar movements and types of muscle contractions.
Conclusions: Bipolar and monopolar CS are safe procedures identifying similar cortical areas as eloquent, although monopolar cortical stimulation is less time consuming.
Significance: Findings advocate the use of monopolar CS in a clinical setting.

1. Introduction

Electrocorticography and cortical stimulation mapping were first used in intraoperative settings and were described in detail by Penfield and colleagues (Penfield and Jasper, 1954). With the advent of subdural electrodes used to map the seizure onset zone prior to epilepsy surgery, extraoperative cortical stimulation mapping has emerged (Nair et al., 2008; Lesser et al., 2011). Extraoperative cortical stimulation mapping is performed outside the operating theatre, once the patient has been implanted with subdural electrodes. Therefore, it has less time constraints when compared to cortical stimulation performed intraoperatively. Despite extraoperative cortical stimulation mapping is being widely used in the presurgical workup of patients with pharmacoresistant seizures, it is not standardized across centres. In some centres adjacent pairs of electrodes are stimulated (bipolar stimulation) whereas in other centres one electrode, referenced to a distant electrode, overlying non-eloquent cortex is stimulated (monopolar stimulation). Bipolar stimulation requires that each electrode is stimulated twice to identify the function underlying each

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electrode. Comparison of current flow during monopolar and bipolar stimulation using a 3-dimensional finite element model of the brain revealed that bipolar adjacent electrodes were found to be very efficient in producing localized current flow (Nathan et al., 1993). Monopolar cortical stimulation produced higher current densities when compared to bipolar stimulation with comparable stimulation current; however, monopolar stimulation also stimulated a larger amount of tissue when compared to bipolar stimulation. How this theoretical model translates into practice remains an open question. More importantly, how these parameters potentially affect the appearance and presence of clinical signs elicited by cortical stimulation remains to be determined. This has important implications for clinical practice and decision making in relation to which part of the cortex can be resected while minimising the risk of postoperative functional deficits.

We therefore examined bipolar versus monopolar cortical stimulation in patients undergoing subdural recording for presurgical evaluation of pharmacoresistant epilepsy. Firstly, we aimed to determine whether there are differences in the number of electrodes eliciting clinical signs and therefore in the anatomical mapping result of eloquent cortex. Secondly, we asked whether these stimulation practices differed with regards to their safety profile and the propensity to generate afterdischarges which can evolve into stimulation induced seizures. Lastly, we investigated whether different modes of stimulation leading to movements are qualitatively different when the same electrode overlying eloquent cortex is stimulated with either bipolar or monopolar cortical stimulation.

2. Methods

We studied 5 patients (3 female, 2 male) in whom presurgical work up included extraoperative cortical stimulation to map eloquent cortex prior to epilepsy surgery. Patients were included in the study if there was coverage of pre- and postcentral gyrus (for an example see Fig. 1A and B). Detailed patient characteristics are outlined in Supplementary Table S1) The study was approved by the local ethics committee and informed consent was obtained from the patients prior to the cortical stimulation procedure, as in our center stimulation procedure may be either bipolar or monopolar based on preference of the consultant in charge All patients had frontal lobe epilepsy (4 left, 1 right).

2.1. Surgical implantation and localization of electrodes

Electrodes were implanted in all patients and coverage was based on the hypothesis of the potential epileptogenic zone which was estimated on seizure semiology and the results of presurgical investigations. We obtained intraoperative photographs to monitor the position of the electrodes (Fig. 1A and B). After the implantation procedure postoperative CT images were obtained. Finally, preimplantation MRI was coregistered (rigid body coregistration) with postimplantation CT with the aim of creating electrode maps on 3D brain surface rendering to localize the implanted electrodes with relation to the brain structures. This coregistration and visualization of the 3-D reconstructions of electrodes coregistered with the preoperative MRI was performed using Amira® software (http://www.vsg3d.com/amira/overview). This is a software for advanced 3D image processing and visualisation. The shortest distance between the center of the discordant electrode and central sulcus was measured (Supplementary Fig. S1).

2.2. Cortical stimulation procedure

Cortical stimulation was performed using both bipolar and monopolar stimulation techniques to identify motor and language areas of cortex underlying the electrode contacts. Previous reports have found that longer stimulus duration and shorter intertrial intervals when stimulating the same electrodes increase the likelihood of afterdischarges (ADs) (Lesser et al., 2008; Lee et al., 2010). The impact of the length of the total stimulation session has not been investigated, but it seems reasonable to assume that it might influence the occurrence of ADs as well. Therefore, monopolar and bipolar stimulations were performed in different sessions with each session lasting less than 80 min. However, in one patient, due to time constraints prior to electrode explantation and resection, monopolar cortical stimulation was performed immediately after bipolar cortical stimulation, with an increase of afterdischarges in the monopolar stimulation session. Therefore this patient was excluded in the analysis of afterdischarges. Additionally the order of bipolar and monopolar stimulation was inverted to avoid a systematic effect of the order (starting with mono- or either bipolar stimulation) on afterdischarges. The other four patients had a break between the sessions of at least 120 min. To avoid stimulation induced seizures, antiepileptic medication was reintroduced prior to cortical stimulation mapping. In both stimulation mode, 5 s trains of 50-Hz unipolar bi-phasic square wave pulses of a AC-current with a pulse with of 500 μs were delivered by a Nicolet™ cortical stimulator used with the C64-OR amplifiers with and Nicolet Cortical stimulator Control unit (ISO 13485, ISO 9001; Nicolet Biomedical, Madison, US). Current intensity was gradually increased from 1 mA in increments of 0.5 or 1 mA up to 7.5, 15 mA peak to peak of the biphasic stimulus, until the occurrence of a clinical sign or afterdischarges (AD) on EEG monitoring. Negative and positive motor symptoms were assessed and patients were asked to report sensations. We screened for language function by asking the patient to read aloud and name objects. If these screening tests were positive, more testing was performed according to our clinical protocol for language mapping. Intracranial EEG was recorded during electrical stimulation using a 128-channel EEG machine (Nicolet Biomedical, Madison, US).

2.3. Stimulation technique and analysis of stimulation responses

Bipolar extraoperative stimulation is not a standardized method and the stimulation procedure varies substantially across centres and examiners. Possible approaches include: (1) Each pair of electrodes can be stimulated, moving across the grid by one electrode (example: pair 1: electrode G1 and 2; pair 2: electrode G2 and 3). (2) Alternatively, two electrodes, which are not far away from each other but still separated by one electrode contact, are stimulated, leading to lower spatial resolution of the stimulation response (pair 1: electrode G1 and 2; pair 2 electrode G3 and 4). In our centre, historically, bipolar mapping was performed by stimulating each adjacent electrode as in method 1, first stimulating each row of electrodes along the horizontal plane (Fig. 1C), and then in a vertical electrode row (Fig. 1D). The function ascribed to cortex underlying each electrode is then inferred from combining results of the stimulations involving that electrode. If two stimulations involving adjacent pairs with one electrode remaining the same, elicit the same clinical sign, then the sign can be attributed to the common electrode.

Monopolar stimulation was performed with the active electrode systematically moving across the electrode array (Fig. 1E), whereas the reference electrode remained the same (Nair et al., 2008; Kombos and Süss, 2009; Lesser et al., 2011). In order to ensure that the elicited sign can be attributed to the active electrode, the reference electrode was tested prior to the monopolar stimulation to ensure that it is not overlying eloquent cortex. In this mode a fixed remote reference electrode is used. Hence, an electrode away from the central sulcus, at the opposite edge of the electrode array, was chosen for this purpose. This distant electrode, referenced to an