Journal of Clinical Neuroscience xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Case study

Threshold and distribution of afterdischarges with electrical cortical stimulation

Hime Suzuki [a], Rei Enatsu [a], Aya Kanno [a], Yuto Suzuki [a], Rintaro Yokoyama [a], Satoshi Ookawa [b], Satoko Ochi [a], Nobuhiro Mikuni [a,*]

[a] Department of Neurosurgery, Sapporo Medical University, Sapporo, Japan
[b] Department of Neurosurgery, Oji General Hospital, Tomakomai, Japan

ARTICLE INFO

Article history:
Received 20 March 2018
Accepted 24 June 2018
Available online xxxx

Keywords:
Afterdischarge
Electric cortical stimulation
Functional brain mapping
Epilepsy
Intracranial electrode

ABSTRACT

Objective: The present study aimed to investigate the threshold and distribution of afterdischarges (ADs) with cortical electrical stimulation for functional brain mapping.
Method: We retrospectively analyzed data from 11 patients with medically intractable epilepsy who underwent 50-Hz cortical electrical stimulation for functional mapping followed by resection. These patients became seizure free for more than six months. The threshold and distribution of ADs induced by the stimulation were evaluated.
Results: The median threshold was 6 mA (range: 2–15 mA) for the frontal lobe, 8 mA (3–15 mA) for the temporal lobe, 6 mA (2–15 mA) for the parietal lobe, and 6 mA (4–12 mA) for the occipital lobe. No significant interlobar differences were observed in AD thresholds. No significant differences were noted between within and outside epileptogenic zones. The distribution of ADs, remote spread was observed in all patients, reflecting fronto-parieto-temporal connections, as well as contiguous spread. The stimulation of premotor areas, the inferior parietal lobule, supplementary motor area, and basal temporal areas appeared to induce ADs in remote cortices.
Conclusion: While no locational differences were observed in AD thresholds, each brain region showed a characteristic pattern for AD spread. Remote AD spread needs to be considered for safe functional mapping.

1. Introduction

Electrical cortical stimulation has become the gold standard for localizing the eloquent cortex, and provides important information for preserving brain function during surgery. In recent studies, electrical stimulation was applied for the intraoperative monitoring of subcortical fibers [1,2].

Electrical cortical stimulation is typically performed using chronically implanted electrodes in patients with drug-resistant epilepsy. High frequency electrical stimulation (e.g. 50 Hz) is commonly employed for functional mapping; however, this type of stimulation may induce electroencephalographic or clinical seizures [3]. Adrian et al. initially reported the electroencephalographic seizure pattern induced by a stimulation in 1936, and termed it an “afterdischarge (AD)” [4]. ADs were found to be induced by cortical stimulation and characterized by transient large amplitude, rhythmic activity [5,6]. The International Federation of Societies for Electroencephalography and Clinical Neurophysiology defines ADs as follows: (1) an EEG seizure pattern following a single or the repetitive electrical stimulation of a discrete area of the brain via cortical or intracerebral electrodes, and (2) a burst of rhythmic activity following a transient such as an evoked potential or spike [7]. Blume et al. reported that the appearance of ADs was elicited in 12% of all stimulated electrodes [5].

However, there have been conflicting findings on the effects of lobar differences and cortical epileptogenicity with the induction of ADs [8,9,10,5,6], and the threshold of AD induction currently remains unclear. ADs not only induce clinical seizures, but also activate a large area of cortical regions, resulting in misinterpretations for functional mapping. Precise information on ADs will be useful for establishing safe and accurate electrical stimulation procedures for functional brain mapping. The present study investigated (1) the stimulation threshold of AD induction and (2) AD distribution.

* Corresponding author at: Department of Neurosurgery, Sapporo Medical University, South1, West16, Chuo-ku, Sapporo 060-8543, Japan.
E-mail address: mikunin@sapmed.ac.jp (N. Mikuni).

https://doi.org/10.1016/j.jocn.2018.06.039
0967-5868/

2. Methods

2.1. Patients

Eleven patients (four females, age: 14–47 years old) with medically intractable focal epilepsies who underwent electrical cortical stimulation with subdural electrodes at the Sapporo Medical University between October 2014 and March 2016 were enrolled in the present study (Table 1). All patients became seizure free for more than six months after focal resection. Ten patients were right handed and one patient (Case 5) was left handed. Subdural electrodes were implanted on the left side in six patients and on the right side in five patients. The type of epilepsy and histopathology and location of epileptogenic zones (EZs) are shown in Table 1. The present study was approved by the Ethical Committee of Sapporo Medical University Graduate School of Medicine (No. 23-161) and written informed consent was obtained from all patients.

2.2. Implantation of chronic subdural electrodes

Subdural electrodes were implanted in the lateral, mesial, and basal aspects of each hemisphere. The grids consisted of two or four rows, with each row containing five to eight platinum electrodes (Unique Medical Co., Ltd., Tokyo, Japan). Electrodes were made of platinum with a recording diameter of 3 mm and an inter-electrode distance of 1 cm. The strip consisted of a single row of six electrodes of the same configuration as that used for grids. The median number of implanted electrodes per patient was 72 (range: 58–104 electrodes). The locations of the implanted electrodes were confirmed using a pre-surgical three-dimensionally reconstructed MRI image coordinated with post-operative high resolution volumetric CT (slice thickness of 1 mm) to provide a visual correlation between each electrode position and the corresponding cortical area or deep structure. The premotor area (PM), supplementary motor area (SMA), and preSMA were defined according to a previous proposal [11,12]. The rostral border of the PM was defined as 30–35, 15–30, and 15–20 mm rostral to the precentral sulcus in the superior, middle, and inferior frontal gyri, respectively [11]. The medial PM or medial Brodmann's area (BA) 6, which is above the cingulate sulcus, was subdivided into preSMA and SMA parts. The vertical anterior-commissural (VAC) line was used as a general landmark to differentiate between preSMA and SMA [12]. The vertical posterior-commissural (VPC) line was also used as an anatomical landmark to differentiate between the SMA and paracentral lobule (PCL) [12].

2.3. Monitoring and mapping

Invasive monitoring with subdural electrodes was performed over seven days in all patients. Spontaneous seizures were recorded for three or four days after implantation, and antiepileptic medication was then restarted. Cortical electrical stimulation was performed thereafter for functional mapping as part of the routine pre-surgical evaluation. Cortical electrical stimulation was performed and analyzed by digital EEG (EEG-1200 Neurofax, NIHON-KOHDEN, Japan). Repetitive square wave electrical currents of alternating polarity with a pulse width of 0.3 ms were delivered at a frequency of 50 Hz for 5 s. All electrodes were stimulated in a bipolar fashion for screening, and the pairs of electrodes that induced clinical symptoms were selected for stimulation in a monopolar fashion for precise localization. The electric current was increased from 0 to 15 mA in 1–2 mA steps until a behavioral response was observed. In the present study, we retrospectively analyzed the data of the bipolar stimulation, and defined rhythmic electricity activity with >5-second duration and >500 μV amplitude as AD (Fig. 1a). The remote spread of ADs was defined as non-contiguous spread in more than two electrodes (>2 cm) apart from the stimulated electrodes. EZs were defined as resected areas to achieve a seizure-free condition, following the previous proposal [13].

2.4. Statistical analysis

The threshold and distribution of ADs induced by the stimulation were evaluated. AD thresholds were analyzed to assess inter-lobar differences and comparisons were conducted between EZs and non-EZs using IBM SPSS Statistics version 22 (IBM Corp., Armonk, NY, USA). The Kruskal-Wallis test was performed for lobar comparisons, and the Mann-Whitney *U* test for comparisons between EZs and non-EZs.

3. Results

3.1. Threshold of ADs

ADs were induced at a median ratio of 72% of electrodes (range: 25.5–96.4%) in each patient (Table 1).

The median AD threshold was 6 mA (range: 2–15 mA, N = 87) for the frontal lobe, 8 mA (range: 3–15 mA, N = 102) for the temporal lobe, 6 mA (range: 2–15 mA, N = 33) for the parietal lobe, and 6 mA (4–12 mA, N = 10) for the occipital lobe. No significant

Table 1
Patient profile.

Case	Age/Sex	Handedness	Diagnosis	Pathology	Epileptogenic zone	Stimulated Pairs	AD(+) electrodes	Remote spread
1	28F	Rt	Lt. FLE	FCD Ib	Lt. PreCG + PM	39	16	8
2	17M	Rt	Lt. FLE	NS	Lt. PCL	28	13	9
3	14M	Rt	Rt. F-TLE	FCD	Rt. F + lat.T	50	25	11
4	39F	Rt	Lt. TLE	HS	Lt. mesial T, Lt. T-P operculum	28	27	12
5	45F	Lt	Rt. TLE	HS	Rt. ant. T	25	18	11
6	22F	Rt	Lt. TLE	NS	Lt. mesial T	29	16	6
7	22M	Rt	Lt. TLE	HS	Lt. ant. T	31	23	14
8	35M	Rt	Lt. TLE	Ganglioglioma	Lt. ant. T	31	23	10
9	47M	Rt	Rt. TLE	HS, FCD	Lt. ant. T	26	23	8
10	31M	Rt	Rt. PLE	Diffuse astrocytoma	Rt. AG	37	32	19
11	43M	Rt	Rt. OLE	NS	Rt.O	47	12	3

AG: angular gyrus, ant: anterior, F: Female, FCD: focal cortical dysplasia, FLE: frontal lobe epilepsy, HS: hippocampal sclerosis, lat: lateral, Lt: Left, M: Male, NS: not specific, O: occipital, OLE: occipital lobe epilepsy, PCL: paracentral lobule, PLE: parietal lobe epilepsy, PM: Premotor area, PreCG: precentral gyrus, Rt: Right, T: temporal, TLE: temporal lobe epilepsy, T-P: temporo-parietal.

Please cite this article in press as: Suzuki H et al. Threshold and distribution of afterdischarges with electrical cortical stimulation. J Clin Neurosci (2018), https://doi.org/10.1016/j.jocn.2018.06.039