The Development of an Automated Single Pulse Electrical Stimulation Protocol to Identify the Seizure Onset Zone in Focal Epilepsy

Tyler Davis MD, PhD; Paul A. House MD
University of Utah, Department of Neurosurgery, Salt Lake City, UT, 84132 USA

Introduction

Identification of the seizure onset zone (SOZ) is a crucial step in the surgical care of patients with partial epilepsy. The SOZ is usually identified through manual analysis of intracranial electrode recordings during spontaneous seizures. Although this approach is the "gold standard", it is costly, time-consuming, and imperfect. Single pulse electrical stimulation (SPES) has been explored as a means of SOZ identification, but previous SPES protocols continue to use manual techniques and show varied results across patient datasets (1-4). We are developing a novel SPES technique to identify the SOZ in an automated and reproducible manner.

Methods

SPES was automatically applied to intracranial ECoG electrodes in 5 patients using a pseudorandom routine with multiple repetitions. Stimulation intensity was set at 3.5 mA using monopolar biphasic pulses of 1 ms duration. Trial-averaged spectrograms were masked for significance ($p<0.05$) and used to assign values to each electrode based on response strength and time-frequency pattern. Maps were generated from these values to provide an estimate of the SOZ.

Patient characteristics

Patient #	Implanted Electrodes	Gender	Age	Seizure Onset Zone (SOZ)	Imaging
1	65	F	32	Right posterior middle temporal	Right prior DNET resection showing nodular enhancement
2	114	M	9	Right medial temporal pole	Right middle cranial fossa arachnoid cyst
3	66	M	25	Left deep hippocampal, parahippocampal	Left prior pilocystic astrocytoma resection without recurrence
4	154	F	9	Right cingulate	No abnormalities
5	116	F	29	Left motor, hippocampal, parahippocampal	No abnormalities

Results

Stimulation of electrodes inside the clinically determined SOZ showed suppression of broadband (10-250 Hz) power lasting as long as 1 second on nearby electrodes that were also typically located inside the clinical SOZ (Figure 1a). Suppression was observed outside the SOZ in some patients, but these responses were shorter in duration (figure 1b). Other responses such as broadband activation occurred outside the SOZ.

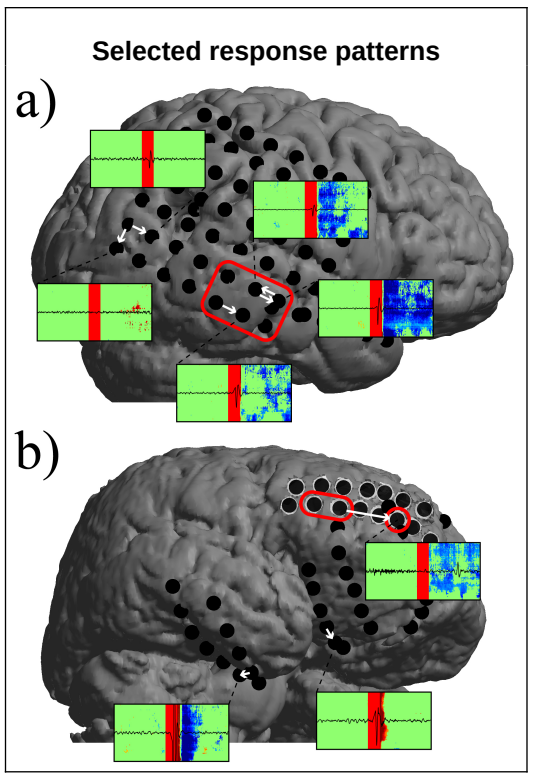

Figure 1. Selected time-frequency responses for patients 1 (a) and 4 (b). Significance-corrected ($p<0.05$) spectrograms are shown from -1 to 1 sec centered on stimulation and 10 to 250 Hz. Stimulation-response pairs are indicated with a white arrow. The clinical SOZ is outlined in red.

The SOZ was estimated by generating maps from the time-frequency responses (Figure 2). Spectrogram values from 0.4 to 1 sec post-stimulation and 70 to 250 Hz were used. Electrodes that both evoked and recorded long-term broadband suppression were assigned a high value. The estimated SOZ demonstrated high specificity for the clinical SOZ (Figure 2a). Multiple clinical onset zones in a patient with normal imaging were also correctly identified (Figure 2b).

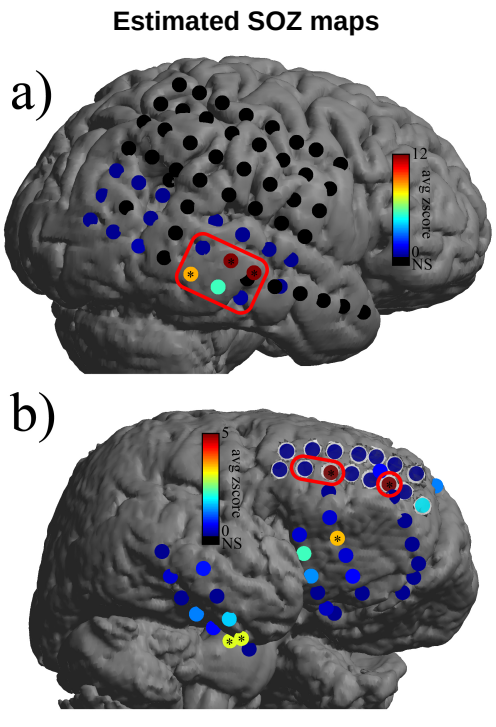

Figure 2. SPES response maps of the estimated SOZ for patients 1 (a) and 4 (b). Electrode color indicates the magnitude of suppression calculated from normalized and significance-corrected ($p<0.05$) spectrograms. Black electrodes did not receive SPES. Asterisks indicate >50% of max and are considered the estimated SOZ.

The estimated SOZ significantly ($p<0.05$) identified the clinical SOZ in 4 of the 5 patients.

Patient results

Patient #	Analyzed Electrodes	Sensitivity	Specificity	p-Value
1	19	**0.50**	**1.00**	**0.021**
2	90	**1.00**	**1.00**	**<0.001**
3	66	**0.70**	**0.96**	**<0.001**
4	72	**0.67**	**0.95**	**0.014**
5	92	0.40	0.93	0.058

Table 2. Results by patient. Bold values are significant ($p<0.05$, Fisher Exact).

Conclusions

Our results, while preliminary, are encouraging. Identification of the SOZ is rapid, reproducible, and specific, which suggests that our approach, if validated, may be useful for clinical care.

Learning Objectives

Participants should be able to discuss the development of a novel stimulation paradigm to identify seizure onset zone.

References

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