

Multi-component intrinsic brain activities as a safe, alternative to cortical stimulation for sensori-motor mapping in neurosurgery

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Abstract

Objective: To assess the feasibility of multi-component electrocorticography (ECoG)-based mapping using “wide-spectrum, intrinsic-brain activities” for identifying the primary sensori-motor area (S1-M1) by comparing that using electrical cortical stimulation (ECS).

Methods: We evaluated 14 epilepsy patients with 1514 subdural electrodes implantation covering the perirolandic cortices at Kyoto University Hospital between 2011-2016. We performed multi-component, ECoG-based mapping (band-pass filter, 0.016–300/600 Hz) involving combined analyses of the single components: movement-related cortical potential (<0.5–1Hz), event-related synchronization (76–200 Hz), and event-related de-synchronization (8–24 Hz) to identify the S1-M1. The feasibility of multi-component mapping was assessed through comparisons with single-component mapping and ECS.

Results: Among 54 functional areas evaluation, ECoG-based maps showed significantly higher rate of localization concordances with ECS maps when the three single-component maps were consistent than when those were inconsistent with each other ($p < 0.001$ in motor, and $p = 0.02$ in sensory mappings). Multi-component mapping revealed high sensitivity (89–90%) and specificity (94–97%) as compared with ECS.

Conclusions: Wide-spectrum, multi-component ECoG-based mapping is feasible, having high sensitivity/specificity relative to ECS.

Significance: This safe (non-stimulus) mapping strategy, alternative to ECS, would allow clinicians to rule in/out the possibility of brain function prior to resection surgery.

Key words:

Movement-related cortical potential, event-related synchronization, event-related de-synchronization, electrocorticography, primary sensory area, primary motor area

1. Introduction

Functional brain mapping for precise identification of the primary sensori-motor area (S1-M1) prior to epilepsy surgery is important for reducing the risk of postoperative functional deficits. Electrical cortical stimulation (ECS) mapping has remained the gold standard for preoperative functional mapping in patients with refractory focal epilepsy¹⁻⁴. However, ECS is limited by the induction of after-discharges and stimulation-induced seizures that introduce a source of error in the detection of functionally important zones, including S1-M1⁵. These limitations can be overcome by functional mapping based on intrinsic-brain activities using electrocorticography (ECoG). ECoG components assessing different spectral activities include movement-related cortical potentials (MRCP)^{6,7}, event-related synchronization (ERS), and event-related de-synchronization (ERD)^{8,9}. Mapping based on each of these components individually has revealed that intrinsic-brain activity plays supplementary roles of ECS mapping^{7,10-12}. It is essential to comprehensively reflect the various spectrum intrinsic-brain activities associated with neural processing; however, the accuracy and feasibility of mapping based on the combination of MRCP/ERS/ERD have not been examined.

Given the specificity/sensitivity of MRCP/ERS/ERD, we hypothesized that mapping based on a combination of these components, “ECoG-based mapping”, would provide the evaluation of brain function in even greater detail than that by using each component alone. Higher levels of specificity/sensitivity will contribute to more reliable clinical decisions about the resection margin (specifically, to “rule in/out” a given area of interest according to its suspected function). To this end, the present study aimed to compare multi-component, ECoG-based mapping (“multi-component mapping”) with single-component ECoG-based mapping (“single-component mapping) and ECS.

2. Methods

2.1. Patients

We recruited patients with focal epilepsy who underwent subdural electrode implantation for presurgical evaluation at Kyoto University Hospital between January 2010 and July 2016. Inclusion criteria were (i) implantation of subdural electrodes covering the perirolandic cortices

and (ii) completion of ECoG-based mapping for at least three motor tasks. Fourteen patients (five females and nine males; mean age, 34.2 years; age range, 16–61 years) were enrolled in this study. A total of 53 motor tasks (three to five tasks per patient) contralateral to the implanted electrodes were executed and analyzed. After explaining the purpose and potential risks of the study, written informed consent was obtained from all patients. This study was approved by the ethics committee of Kyoto University Graduate School of Medicine (No. C533).

2.2. ECoG monitoring and recording conditions

All patients underwent subdural electrode implantation and 2-week ECoG monitoring to determine seizure onset zone and to define functionally important areas prior to epilepsy surgery. Subdural electrodes had a 2.3 or 3 mm of recording diameter with a center-to-center interelectrode distance of 5 mm and 1 cm (ADTECH, WI, USA and Unique Medical Co., Ltd., Tokyo, Japan). ECoG was recorded using EEG1100 or EEG1200 (Nihon Kohden, Tokyo, Japan) with the bandpass filter set at 0.016–300/600 Hz depending on the sampling rate (1000 or 2000 Hz). All subdural electrodes were referenced to a scalp electrode (Unique Medical Co., Ltd., Tokyo, Japan) placed on the skin of the mastoid process contralateral to the implanted side.

2.3. Motor tasks

For multi-component mapping, patients were asked to repeat brisk self-paced movements at intervals of 8–10 s without counting the number and interval of movements by the patient. Three to five motor parts were selected for motor tasks based on the clinical purpose according to the extent of electrode coverage as follows. The details of the recording process have been described previously^{10, 13}.

2.4. Anatomical localization of subdural electrodes in pre-central and post-central gyri

All patients underwent MRI at a field strength of 1.5 T (Avanto, Siemens, Erlangen, Germany) while subdural electrodes were in place during ECoG monitoring. We determined the location of each electrode, including precentral sulcus (PrCS), pre-central gyrus (PrCG), or central sulcus

(CS), post-central gyrus (PoCG), post-central sulcs (PoCS), using the signal void created by the electrode metal¹⁴.

2.5. Data analysis

ECoG and EMG data were processed in an off-line manner using customized MATLAB (MathWorks, Natick, MA, USA) scripts. All recorded data were averaged time-locked to the EMG onset, visually determined in the off-line analyses. The analysis window for all the components of ECoG mapping was set from 4.0 s before EMG onset to 2.0 s afterwards. The baseline period was defined as the first 10% of the analysis window (from 4.0 to 3.4 s before EMG onset).

2.6. Movement-related cortical potentials

To clarify the time course of slow potentials for analyzing MRCP, data were low-pass filtered at 10 Hz and averaged. After confirming the reproducibility of averaged waveforms between two the ensembles, we produced averaged waveform of all the sessions for each task^{7, 10, 13}.

We defined S1-MRCP as electrodes located on the anatomical sensory area (PoCG, PoCS, or CS) and representing RAP without the pre-movement component. To evaluate the existence of each of the four components in MRCP, we evaluated the onset time and peak amplitude¹⁵. The mean \pm 2 standard deviations (SD) during the baseline period were defined as thresholds¹⁵.

2.7. Event-related synchronization and de-synchronization

The time-frequency representation of ECoG power was calculated using a short-time Fourier Transform (STFT) with a Hanning window of 250 or 500 points (time resolution of 250 ms and frequency resolution of 4 Hz) depending on sampling rate at each 10-ms step. Data were averaged across trials and converted to the logarithmic scale (base 10), then averaged data of baseline power were subtracted for each 4 Hz frequency band^{16, 17}. M1-ERS was defined as follows: 1) electrodes located on PrCG, PrCS, or CS, 2) proportional power increase (ERS) in the frequency band of 76–100 Hz, 100–200 Hz, or both, in relation to threshold values (mean \pm 3

SD power values during the baseline period), and 3) the onset time of ERS preceding that of EMG. M1-ERD was defined similarly, but with a proportional power decrease (ERD) in the frequency band of 8–12 Hz, 16–24 Hz, or both.

2.8. Electrical cortical stimulation

Repetitive, square-wave electric currents of alternating polarity with a pulse width of 0.3 ms and frequency of 50 Hz were delivered through a pair of electrodes for 1–5 s (electrical stimulator SEN-7203, MEE-1232, and MS-120B; Nihon Kohden, Tokyo, Japan). Additional details regarding ECS methods have been described elsewhere^{10, 18}.

2.9. Assessment and statistics

The primary measure was task-driven consistency among multi-component mapping (MRCP/ERS/ERD) for M1 determination, with results classified into two groups for each motor task as follows: if the M1 site detected by all three components (MRCP/ERS/ERD) contained an overlapping site, the M1 was classified as “consistent M1”; if the overlapping sites were shared among less than all three components, the M1 was classified as “inconsistent M1.”

The secondary measure was ECoG-ECS based functional mapping concordance, i.e., task-driven localization concordance between M1 determined by multi-component mapping (overlapping sites of MRCP/ERS/ERD) and that determined by ECS mapping (ECS-positive sites). Concordance was assessed in each combination of multi-component mapping and divided into four categories for each task, as follows: 1) highly concordant (ECoG component-based mapping sites completely matched corresponding ECS-positive sites), 2) partially concordant (ECoG component-based mapping sites partially matched corresponding ECS-positive sites, or ECS-positive sites were adjacent to ECoG component-based mapping sites), 3) discordant (ECS-positive sites were remote from ECoG-based mapping sites by a distance of more than one electrode, or 10 mm), or 4) absence of ECS-positive sites.

Finally, we measured electrode-driven sensitivity, specificity, and predictive values of ECoG component-based mapping against ECS for identifying M1 (i.e., ECS-positive site was

defined as a true positive site). All statistical analyses were performed using JMP software (JMP Pro version 12; SAS Institute, Cary, NC).

3. Results

3.1. Multi-component map consistency and ECoG-ECS concordance

In total, 53 tasks were evaluated. Of those, M1-MRCP, M1-ERS, and M1-ERD were observed in 68% (36/53), 60% (32/53), and 89% (47/53) of tasks, respectively, and S1-MRCP, S1-ERS, and S1-ERD were observed in 58% (31/53), 75% (40/53), and 85% (45/53) of tasks, respectively. Somatotopically-corresponding regions for ECS-positive responses to motor tasks were observed in 68% (36/53) of tasks in M1 maps and 60% (32/53) of those in S1 maps. A Venn diagram was created to assess the number of motor tasks exhibiting ECoG component-based map consistency and ECoG-ECS concordance. Consistent M1 and S1 were observed in 47% (25/53) of M1 and 55% (29/53) of S1 maps, respectively. The ratio of ECoG-ECS concordance (including high concordance and partial concordance) in consistent M1 and S1 were significantly higher than those in inconsistent M1 and S1 (22/25 [88%] vs 10/28 [36%], $p < 0.001$ and 18/29 [62%] vs 7/21 [30%], $p = 0.02$, respectively). None of the motor tasks negative on ECoG component-based maps were ECS-positive. By contrast, 17 tasks in M1 and 18 tasks in S1, were MRCP-positive, ERS-positive, and/or ERD-positive, but ECS-negative. One motor task in M1 and three motor tasks in S1 were negative for both ECS and all ECoG component-based maps.

3.2. Electrode-driven sensitivity and specificity of multi-component mapping

In single component mapping, ERD showed the highest sensitivity among the three components (76% in M1 and 82% in S1), whereas MRCP showed the highest specificity (92% in M1 and 83% in S1). Multi-component mapping substantially increased the sensitivity and specificity. The union of MRCP/ERS/ERD produced higher sensitivity values (89% in M1 and 90% in S1), and the intersection of MRCP/ERS/ERD produced markedly high specificities (97% in M1 and 94% in S1) and highly correct classification (89% in both M1 and S1) relative to single-component mapping.

4. Discussion

Numerous studies have explored the relationship between intrinsic-brain activity and brain function, although ECS remains the gold standard for clinical brain mapping. Especially, the two points are very unique; 1) it employed not only fast activities both also very slow cortical components only recorded by long time constant such as 10 sec, and 2) those components were directly compared with ECS. The key findings from this study were as follows: (i) among the three ECoG components compared with ECS, MRCP (slow component) had the highest spatial specificity and ERD had the highest spatial sensitivity; (ii) multi-component mapping yielded higher sensitivity and specificity values than single-component mapping; (iii) significantly higher ECoG-ECS concordances in S1-M1 mapping were observed by multi-component mapping, suggesting that ECoG-based mapping is comparable to ECS for determining M1-S1 sites in situations of consistent M1/S1; and (iv) consistent M1/S1 sites were specifically identified by “latter part of MRCP component” (a part of component) and power degree of ERS/ERD, which may suggest a stronger association between the neural population and motor area activation as compared with that in non-consistent M1/S1. These findings support our hypothesis that wide-spectrum, ECoG-based mapping should combine multiple components in order to achieve highly accurate brain mapping. Given the properties of high sensitivity and specificity, multi-component mapping would allow clinicians to rule in/out the likelihood of brain function prior to resection surgery, and is thus widely applicable for preoperative evaluations in brain surgery, even besides epilepsy surgery.

Compared to previous studies that assessed the sensitivity and specificity of ECoG-based mapping relative to ECS mapping^{11, 12, 19, 20}, the significance of our findings is highlighted by the high specificity of multi-component mapping and the large number of patients. Differences in experimental conditions between the previous studies and our study should be discussed as follows in two points. First, the definitions of ERS/ERD differed in terms of power degree. Second, the analyzed ERS/ERD frequency bands differed across studies. Third, previous studies

measured sensitivity and specificity based on electrode units ^{11, 21-23}.

The present study has several limitations. 1) First, our patients suffered from refractory focal epilepsy, and thus there were distortion and limitations in the extent of the coverage by the electrode grid and anatomical configurations. 2) Second, intrinsic activity may be subject to several factors. 3) Finally, while our study highlights the feasibility and usefulness of ECoG-based mapping, its superiority (rather than non-inferiority) to ECS might be difficult to demonstrate as the surgical outcome because we could not conduct randomized control comparison with and without resection of the motor area.

5. Conclusions

Wide-spectrum, multi-component ECoG-based mapping is useful to define the S1-M1 based on its high sensitivity and specificity relative to ECS, without carrying the risk of stimulation-induced complications. Our findings collectively suggest that wide-spectrum, multi-component ECoG-based mapping is a feasible alternative to ECS.

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