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Abstract. The seizure onset zone (SOZ) and propagation pathways in supplementary motor area (SMA) seizures are difficult to identify because of the short duration and swift propagations of this seizure type. Herein, we studied ictal cerebral blood flow changes, seizure electrical activities, and clinical signs employing simultaneous near-infrared spectroscopy (NIRS) and electrocorticography (ECoG) recordings in a brain tumor patient with SMA seizures. Increased cerebral blood flow was observed from the SOZ in the ipsilateral SMA and spread to the ipsilateral premotor cortex, ipsilateral sensorimotor cortex, and also the contralateral hemisphere. These propagation patterns were concordant with ictal ECoG seizure activities and clinical signs. Removal of the SOZ and surrounding areas, where the higher blood flow and higher frequency oscillations had been identified, achieved a good outcome for this patient. Our ictal NIRS-ECoG technique is robust and useful for detecting the SOZ and seizure propagations.
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Keywords: near-infrared spectroscopy; electrocorticography; ictal high-frequency oscillations; supplementary motor area seizures.

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1 Introduction

Supplementary motor area (SMA) seizures are characterized by sudden, brief tonic posturing of the extremities, vocalization, and initially preserved consciousness.[1] Because the SMA has multiple reciprocal connections to the primary motor cortex, the anterior cingulate gyrus and various parietal sensory areas,[2] the epileptogenic activity can be widespread, with rapid propagation to adjacent structures. Localization of the seizure onset zone (SOZ) may therefore be difficult to establish in SMA seizures, particularly those with no identified structural lesions. Although previous studies used ictal single-photon emission computed tomography (SPECT) to investigate localization of the SOZ and ictal cortical propagation patterns in patients with SMA seizures,[3–5] it is not possible with SPECT to evaluate cortical hemodynamic changes for the entire time period from the preictal phase to the postictal phase.

Near-infrared spectroscopy (NIRS), which measures real-time hemodynamic changes considered to be linked to underlying neural activities,[6,7] has recently been used to monitor rapid cortical hemodynamic changes in patients with epilepsy.[8,9] The better temporal resolution of NIRS overcomes the aforementioned limitation of SPECT. Additionally, our recent studies have demonstrated that simultaneous NIRS and electroencephalographic (EEG) analysis provides useful information about neural networks.[10] We also focused on ictal high-frequency oscillations (HFOs) in electrocorticography (ECoG), which are reportedly specific for detecting the SOZ and allow visualization of dynamic ictal changes.[11] This is the first report, to our knowledge, describing successfully obtaining simultaneous NIRS and ECoG recordings during an ictal event in a patient with SMA seizures.

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2 Material and Methods

The patient was a 9-year-old girl with normal growth. At age 7, she began to have seizures with open eyes, deviation of the head to the right, tonic extension of both arms and the right leg, and tonic flexion of the left knee while remaining conscious. The seizures always appeared abruptly with or without auras. The seizure durations ranged from a few seconds up to approximately 1 min. The seizures were refractory to aggressive pharmacologic treatment, occurring two to three times daily, mainly during the night. Magnetic resonance imaging (MRI) revealed a right medial frontal mass lesion which showed isointensity on a T1-weighted image and hyperintensity on a T2-weighted image, suggesting a dysembryoplastic neuroepithelial tumor (DNT) [Fig. 1(a)]. Following the implantation of electrodes on the right frontal cortex, long-term video/ECoG monitoring, cortical mapping, and simultaneous NIRS and ECoG recordings were obtained.

Subdural electrodes (5×4 and 2×5) were implanted over the right frontal convexity and subdural strip electrodes (1×4 and 1×8) were placed on the right mesial surface so as to cover the SMA, which we speculated to be involved in the patient's seizures [Fig. 1(b)]. The individual electrode contacts were 3.0 mm in diameter platinum discs with a center-to-center electrode distance of 10 mm. The ECoG was recorded employing EEG 1000 (Nihon Koden, Tokyo, Japan) using a bandpass filter set to 0.16 to 300 Hz with a sampling rate of 1000 Hz and an averaged reference from two channels in a relatively silent area of the grid. A 60-Hz notch filter was applied to all channels.

Cortical mapping performed to localize essential brain regions was limited to mesial areas of the right hemisphere in view of invasiveness and possible seizure risk. Stimuli consist of 50 Hz, 0.2 ms, and a repetitive square wave pulse with a

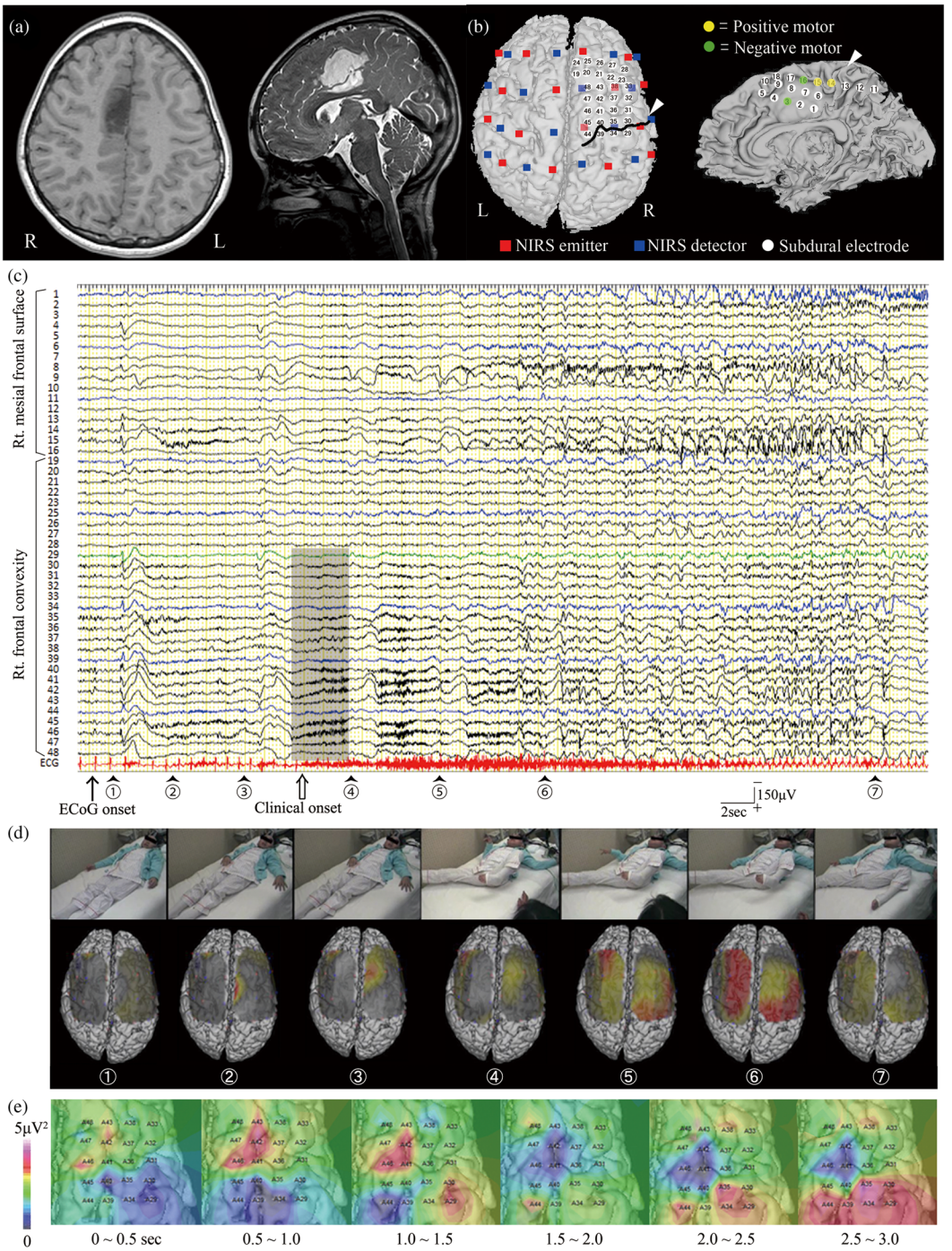

Fig. 1 Results of the ictal NIRS-ECoG study. (a) Preoperative magnetic resonance T1-weighted axial and T2-weighted sagittal images, showing a significant lesion extending to the right supplementary motor area. The characteristic appearance of iso T1 and high T2 signal intensity indicates a dysembryoplastic neuroepithelial tumor. (b) Placement of NIRS probes and subdural electrodes, and the results of cortical mapping. The bilateral motor associated frontal surfaces were sufficiently covered by the placed probes. The central sulcus is indicated by the thick black line and white arrowheads. Eighteen electrodes, each assigned numbers from 1 to 18, covered the right mesial surface and 30 electrodes, each assigned numbers from 19 to 48, covered the right frontal convexity. Each electrode number corresponds to those in Fig. 1(c) and 1(e). Positive motor areas (electrodes depicted in yellow) and negative motor areas (electrodes depicted in green) were identified on the right mesial frontal surface. (c) Ictal ECoG, demonstrated with a reference montage (averaged reference from electrodes #17 and #18). Ictal ECoG onset (black arrow) started with low amplitude fast activity predominantly at #46, determined to be a SOZ from interictal ECoG, approximately 8 s before clinical onset (white arrow) and followed by sharp-slow complexes predominantly at the SOZ (#46) and the neighboring premotor cortex (#41 to #43, #47 and #48). As the seizure entered the tonic phase, epileptic discharges showed higher amplitude, spread diffusely, and lasted longer (up to 17 s). A 3-s epoch (shaded in grey) at 20 electrodes (#29 to #48), where the most prominent HFOs were obtained, was placed for making the topographic images of the averaged powers as shown in Fig. 1(e). (d) Consecutive topographic images on ictal NIRS (lower row) and the corresponding seizure appearance (upper row). Each number (① through ⑦) corresponds to the numbers in Fig. 1(c), shown above. See text for details. (e) Consecutive 3-s topographic images, showing that high-power HFOs (80 to 220 Hz) start at the SOZ (#46) and PMC (#41 to #43), then shift to the SMC (#29, #30, #34, #35, #39, and #44) 1.5 to 2 s later. Intriguingly, this propagation pattern was very similar to that of the right hemisphere in the NIRS study, starting at the SOZ (②), and the right PMC (③) and then continuing to the right SMC (⑤) as shown in Fig. 1(d).

duration of 5 s. The results of cortical mapping are shown in Fig. 1(b). No after-discharges were observed during the session.

For identifying HFOs, the oscillation frequencies before and during clinical onset were determined by time–frequency analysis using EMSE (Source Signal Imaging, San Diego). Clearly, detectable HFOs (80 to 220 Hz) were obtained during the initial 3 s after clinical seizure onset over the SOZ and the surrounding motor associated areas. To analyze propagation of the HFOs in this 3-s epoch, the power spectra were calculated with a frequency of 1 Hz and a temporal resolution of 500 ms for each electrode, and these averaged powers were topographically superimposed on the patient's brain surface image, using Insight (Persyst, Prescott, AZ). These procedures were described in detail elsewhere.[11]

NIRS was carried out with a 695/830 nm spectrometer (ETG–7100; HITACHI Medical, Japan). For each hemisphere, eight emitters and eight detectors were alternately placed on a head shell constituting 24 channels covering the bilateral motor–associated areas including the areas of subdural electrode placement [Fig. 1(b)]. The interprobe distance was 3 cm, and the sampling rate was 10 Hz. The clinical seizure onsets were obtained from initial remarkable electromyographic changes in the patient's arms. The data analysis was performed using MATLAB (The Math Works version 7.1) and NIRS-SPM software.[12] The raw hemodynamic signals were normalized with a 10-s preictal time and filtered using a bandpass filter with a range of 0.02 to 0.4 Hz. Relative changes in oxyhemoglobin, deoxyhemoglobin, and total hemoglobin concentrations were obtained for each channel. Independent component analysis was used to identify and remove motion artifacts and scalp blood flow interference. This method was described in detail elsewhere.[13] Channel positions were superimposed onto the patient's own three-dimensional magnetic resonance images of the brain surface, and finally, the topographic images were obtained.[14] To focus on the changes in cerebral blood flow, only total hemoglobin changes are presented.

3 Results

The ictal NIRS-ECoG results are summarized in Fig. 1(c)–1(e). NIRS results suggest that cerebral blood flow started to rise in the SOZ about 2 s after ECoG onset and peaked 5.6 s after ECoG onset. Subsequently, hemodynamic activations occurred earlier in the right premotor cortex (PMC) (6.5 s after ECoG onset; the same applies hereafter) than in the right sensorimotor cortex (SMC) (13.8 s). Immediately thereafter, the left PMC (14.6 s) and then the left SMC (18.2 s) were activated. These hemodynamic propagation courses were well matched with the spread of seizure electrical activities and the consecutive processes of seizure appearance, beginning with head deviation to the right, tonic extension of the left arm and tonic flexion of the left knee, followed by tonic extension of the right arm and leg [Fig. 1(c) and 1(d)].

Furthermore, topographic maps of HFOs power spectra obtained from initial 3 s at clinical onset [gray shaded area in Fig. 1(c)] showed the propagation of ictal seizure activity, which started from the SOZ, then shifted to the right PMC and finally the right SMC [Fig. 1(e)]. Interestingly, this pattern was remarkably similar to the NIRS study results [Fig. 1(d)] though their temporal ranges were different.

These findings suggested that the SOZ in the right SMA contained an epileptogenic lesion. Accordingly, we performed a partial resection, including the SOZ and the right PMC where higher HFOs and increased cerebral blood flow had initially appeared. Histopathological study of the tumor revealed DNT, consistent with the preoperative diagnosis. Her seizure frequency decreased markedly to once or twice a month postoperatively.

4 Discussion

In this study, increased cerebral blood flow over the SOZ started about 2 s after ECoG seizure onset and hemodynamic activity propagated rapidly to adjacent regions. Rapid reactions such as these have prevented previous ictal SPECT studies from identifying the SOZ and the propagation pattern of seizure activity.[3–5] Our NIRS-ECoG approach overcame this limitation and provided useful information about the SOZ, neural connectivity, and seizure propagations. However, there is no direct evidence that the initial hemodynamic response over the SOZ corresponded to ECoG onset and it seemed to be somewhat shorter than typical vascular responses. The possibility cannot be ruled out that its origins were other seizure activities that had already occurred prior to ECoG onset, such as direct current potentials,[15] which could not be evaluated in this study. Further studies are required to address this issue.

What is the explanation for the NIRS signals being measurable through a subdural grid electrode sheet? While a sheet consists of clear silicon rubbers which have good transmission at near-infrared wavelengths, the metal comprising the electrode absorbs near-infrared light. In this study, the NIRS probes were placed so as to avoid overlapping with the electrodes as much as possible to minimize the amount of near-infrared light absorbed by the electrodes. Furthermore, the fact that NIRS allows the evaluation of "relative" hemodynamic changes also supports the validity and effectiveness of our results even if a small amount of near-infrared light were to be absorbed or scattered by a subdural grid.

As the seizure electrical activity spread outward from the SOZ progressively engulfing the ipsilateral PMC and SMC in the ECoG study, cerebral blood flow increased over the SOZ, then the ipsilateral PMC and finally the ipsilateral SMC in the NIRS study. These results are consistent with known anatomical interconnections between the SMA and the ipsilateral PMC and SMC and facilitated preoperatively determining the areas to be removed. Furthermore, the NIRS study revealed significant propagation to the contralateral PMC and SMC, suggesting transcallosal connections between the SMA of one hemisphere and the opposite PMC as well as cortico-cortical connections between the PMC and SMC. These propagations were also in agreement with the clinical appearance of the seizure as shown in the tonic posturing from left to right.

In epilepsy patients, HFOs have been recognized as important and useful for detecting the SOZ and ictal propagations.[11] To our knowledge, the current study is the first to analyze ictal HFOs simultaneously with hemodynamic evaluation in a patient with SMA seizures. Ictal HFOs were more prominent over the SOZ and the ipsilateral PMC, judged to be the sites of epileptogenic lesions. The removal of these lesions achieved a good outcome for this patient. Furthermore, it is noteworthy that the propagation patterns of ictal HFOs in about 3 s were quite similar to those of the ictal NIRS study at about 1 min. There is presumably an explanation for the difference in temporal ranges between HFOs and NIRS studies. The hemodynamic changes produced by HFO activities might be too small to be detectable using NIRS. In fact, the only significant changes observed in NIRS were those associated with the ictal electrical

activities in the SOZ or the spread of electrical activities driving major seizures, which were large enough for NIRS analysis. The addition-averaging of numerous NIRS signals caused by HFOs might be an option. Although these two propagations had a different time axis, the similar propagations involving the same areas are almost certainly repeated in the ictal phase. Further studies are needed to clarify this issue.

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