

Case Report

Cortico-cortical activity between the primary and supplementary motor cortex: An intraoperative near-infrared spectroscopy study

Masafumi Fukuda, Tetsuro Takao, Tetsuya Hiraishi, Hiroshi Aoki, Ryosuke Ogura, Yosuke Sato, Yukihiro Fujii

Department of Neurosurgery, Brain Research Institute, University of Niigata, Niigata-City, Japan

E-mail: *Masafumi Fukuda - mfuku529@bri.niigata-u.ac.jp; Tetsuro Takao - takao@bri.niigata-u.ac.jp; Tetsuya Hiraishi - tetsuya_hiraishi@me.com; Hiroshi Aoki - aoki1123@bri.niigata-u.ac.jp; Ryosuke Ogura - oguryou@bri.niigata-u.ac.jp; Yosuke Sato - yosuke0420@hotmail.com;

Yukihiro Fujii - yfujii@bri.niigata-u.ac.jp

*Corresponding author

Received: 18 August 14 Accepted: 02 January 15 Published: 24 March 15

This article may be cited as:

Fukuda M, Takao T, Hiraishi T, Aoki H, Ogura R, Sato Y, et al. Cortico-cortical activity between the primary and supplementary motor cortex: An intraoperative near-infrared spectroscopy study. *Surg Neurol Int* 2015;6:44.

Available FREE in open access from: <http://www.surgicalneurologyint.com/text.asp?2015/6/1/44/153872>

Copyright © 2015 Fukuda M. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Background: The supplementary motor area (SMA) makes multiple reciprocal connections to many areas of the cerebral cortices, such as the primary motor cortex (PMC), anterior cingulate cortex, and various regions in the parietal somatosensory cortex. In patients with SMA seizures, epileptic discharges from the SMA rapidly propagate to the PMC. We sought to determine whether near-infrared spectroscopy (NIRS) is able to intraoperatively display hemodynamic changes in epileptic network activities between the SMA and the PMC.

Case Descriptions: In a 60-year-old male with SMA seizures, we intraoperatively delivered a 500 Hz, 5-train stimulation to the medial cortical surface and measured the resulting hemodynamic changes in the PMC by calculating the oxyhemoglobin (HbO₂) and deoxyhemoglobin (HbR) concentration changes during stimulation. No hemodynamic changes in the lateral cortex were observed during stimulation of the medial surface corresponding to the foot motor areas. In contrast, both HbO₂ and HbR increased in the lateral cortex corresponding to the hand motor areas when the seizure onset zone was stimulated. In the premotor cortex and the lateral cortex corresponding to the trunk motor areas, hemodynamic changes showed a pattern of increased HbO₂ with decreased HbR.

Conclusions: This is the first reported study using intraoperative NIRS to characterize the epileptic network activities between the SMA and PMC. Our intraoperative NIRS procedure may thus be useful in monitoring the activities of cortico-cortical neural pathways such as the language system.

Key Words: Cortico-cortical activity, epilepsy, hemodynamic change, near-infrared spectroscopy, primary motor cortex, supplementary motor area

Access this article online**Website:**

www.surgicalneurologyint.com

DOI:

10.4103/2152-7806.153872

Quick Response Code:

INTRODUCTION

Supplementary motor area (SMA) seizures are short in duration and characterized by abrupt, bilateral, tonic

posturing of the extremities, and vocalization without loss of consciousness.^[6] Epileptic discharges from the SMA can rapidly propagate through the primary motor cortex (PMC), anterior cingulate cortex (ACC),

and various parietal somatosensory areas, which form multiple reciprocal connections to the SMA.^[2,4] Better understanding of the mechanisms of SMA propagation can be achieved through improved methods to probe cortical network activities associated with epileptic discharges from the SMA. For example, an ictal single photon emission computed tomography study indicated that seizure-associated hyperperfusion areas did not localize within the SMA, but rather spread to adjacent cortical regions ipsilateral to epileptic foci, such as the ACC and PMC.^[1] Recently, we demonstrated using simultaneous transcranial near-infrared spectroscopy (NIRS) and electrocorticography (ECoG) recordings in a patient with SMA seizures that increased cerebral blood flow was observed from the epileptic discharges in the ipsilateral SMA and spread to the ipsilateral premotor cortex and PMC as well as the contralateral hemisphere.^[7]

In a patient with SMA seizure, we used a novel 4-probe device attached to the brain surface to conduct intraoperative NIRS from four probes to show increased blood flow in the PMC elicited by stimulation to the SMA. This is the first report to determine that intraoperative NIRS can reveal the cortico-cortical activities between the SMA and PMC. Moreover, by placing probes on the brain surface, we were able to obtain greater resolution than with transcranial NIRS methods. Our technique will thus allow improved mapping of cortico-cortical network activities intraoperatively.

CASE REPORT

A 60-year-old male presented with seizures a few months before admission to our hospital. His seizures were characterized by tonic posturing in the left extremities and occurred 3–4 times monthly. T2-weighted magnetic resonance (MR) imaging revealed a high intensity lesion in the medial surface of the right frontal lobe. The lesion was not enhanced by Gd on the T1-weighted MR images, and was suspected to be a low-grade glioma. In order to confirm the relationship between the lesion and the PMC corresponding to the lower extremities, subdural grid electrodes were placed to cover the lateral and medial surfaces adjacent to the PMC. Video-ECoG monitoring demonstrated seizure onset at the right medial surface corresponding to the SMA. The seizure activities rapidly propagated from the SMA to the lateral cortex, including the PMC.

Cortical electrical stimulation was performed for functional cortical mapping. A repetitive square wave with electrical currents of alternating polarity, a pulse width of 0.2 ms, and a frequency of 50 Hz were delivered for 5 s (Nihon Koden, Corporation, Japan). Two neighboring electrodes, with an intensity of 2–5 mA, were stimulated in a bipolar manner. Positive motor and sensory areas were identified by positive motor response (i.e. muscle

twitch) and subjective sensory sensation, respectively. To define the precise location of each electrode on the surface of the brain, subdural electrodes extracted from computed tomography (CT) images were co-registered to three-dimensional volume-rendered MR images (3.0 T) using image-analysis software (Zed-View, LEXI, Inc., Japan). The results of this functional cortical mapping are depicted in Figure 1. Cortical stimulation to the anterior and posterior areas of the seizure onset zone induced habitual seizures.

Before a partial resection of the lesion for pathology, intraoperative NIRS recording was performed upon stimulation of the placed subdural electrodes apparatus of the medial cortical surface. Constant current stimuli, consisting of five rectangular pulses with 2-ms interstimulus intervals, were generated and recorded with a Neuropac (Nihon Koden, Corporation, Japan). The cathode was positioned at Fz. Motor-evoked potentials were recorded from the abductor pollicis brevis and abductor hallucis brevis muscles through paired stainless-steel needle electrodes inserted subdermally. The band-pass filter was set to a range of 5–3000 Hz. The applied stimuli were adjusted to the supra-threshold intensity.

For NIRS monitoring, we developed a novel device comprising of four recording probes spaced 1.5 cm apart and equipped with fixable spatula retractors at the tip of each probe to enable attachment to the brain surface [Figure 2a and b]. The four probes were set to cover the lateral cortex, including the PMC [Figure 2c]. NIRS was carried out with a 695/830 nm spectrometer equipped to our novel monitoring device (ETG-7100; HITACHI Medical, Japan). Emitting light intensity was adjusted to 1 mW (approximately one-fourth

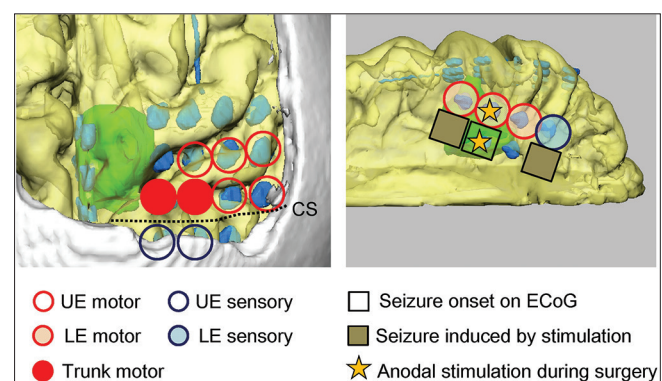


Figure 1: Results of video-electrocorticography (ECoG) monitoring and functional cortical mapping. 3D brain surface images showing recording electrodes (pale blue) and the brain tumor (green). The seizure onset zone (square) was confirmed to reside in the medial surface. The sites in which stimulation induced habitual seizures (closed square) were noted anterior and posterior to the seizure onset zone. Before partial tumor resection, both the foot motor area and seizure onset zone were stimulated for intraoperative NIRS study (stars). UE: Upper extremities, LE: Lower extremities, CS: Central sulcus

of scalp NIRS). The oxyhemoglobin (HbO₂) and deoxyhemoglobin (HbR) concentration changes corresponding to medial surface stimulation in each session were calculated for each segment, which consisted of a 30 s intervals comprising of a prestimulation block (10 s), a stimulation block, and a poststimulation block (20 s). Each session was repeated five times. The present study was approved by the Institutional Review Board Committee at the Niigata University School of Medicine, and informed consent was obtained from the patients (IRB#1559).

In the results, no hemodynamic changes were observed during stimulation of the medial surface corresponding to the foot motor areas at the intensity of 20 mA [Figure 3A]. In contrast, both HbO₂ and HbR increased in the lateral cortex corresponding to the hand motor areas when the seizure onset zone was stimulated at an intensity of 16 mA [b and c in Figure 3B]. In the lateral cortex corresponding to the trunk motor areas and the premotor cortex, hemodynamic changes showed a pattern of increased HbO₂ with decreased HbR [a and d in Figure 3B].

DISCUSSION

To our knowledge, this is the first report using intraoperative NIRS during cortical stimulation to demonstrate cortico-cortical activity between the SMA and PMC. We observed that stimulation of the foot motor area elicited no detectable hemodynamic responses in the lateral cortex, whereas stimulation to the seizure onset zone elicited hemodynamic responses at all four probes despite the stimulation intensity decreasing from 20 to 16 mA. These results likely reflected the epileptic network activities between the SMA and PMC.



Figure 2: (a) Our novel device for the intracranial setting of four NIRS probes. The inter-probe distance was 1.5 cm. (b) Four probes were equipped to the NIRS devices. (c) During surgery, the novel device and its four probes were wrapped by a sterilized cover. The device was fixed by spatula retractors at the tip of each probe for attachment to the brain surface. The probes were placed to cover the lateral cortex including the primary motor cortex

It should be noted that we used high frequency stimulation (5-trains, 500 Hz) in the present study, because we were concerned that 50 Hz-stimulation to the seizure onset zone during surgery and functional mapping might induce seizures. Previously, we characterized hemodynamic connectivity in the language system in a patient with temporal lobe epilepsy.^[8] In this study, 50 Hz-stimulation in the left superior temporal gyrus via subdural electrode contacts gave rise to hemodynamic increases in the inferior frontal gyrus, indicating a strong connection to the stimulation site. In a cortico-cortical evoked potential study,^[5] stimulation of the foot motor cortex elicited responses in the pre- and postcentral gyrus. Thus, 50 Hz-stimulation of the foot motor areas, rather than 500 Hz employed in our present experiments, might induce hemodynamic changes in the lateral cortex as well.

In this study, high frequency stimulation caused the hemodynamic changes characterized by increase in both HbO₂ and HbR in the lateral cortex corresponding to the hand motor areas. This phenomenon was also observed in a study of the language system of the frontal and temporal cortex using simultaneous NIRS and ECoG recordings during cortical stimulation.^[8] In contrast, in the areas corresponding to the trunk motor areas and premotor cortex, hemodynamic changes showed a pattern of increased HbO₂ with decreased HbR as is typical of task-evoked hemodynamic changes. In a previous NIRS study carried out simultaneously with cortical stimulation via subdural electrodes,^[3] 50 Hz-stimulation produced significant increases in both HbO₂ and HbR at the stimulation site and surrounding areas, while 5 Hz-stimulation produced a localized increase in HbO₂ and a decrease in HbR. An increase in HbO₂ with an

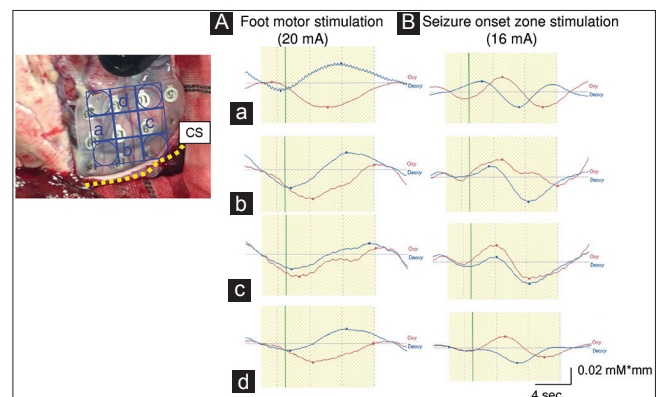


Figure 3: Time course changes of HbO₂ and HbR in the lateral cortex. The left picture shows the relationship between the sites of each of the four probes (circle) and subdural electrodes. Recording sites of NIRS were a, b, c, and d. CS: Central sulcus. (A) No hemodynamic changes were noted in any sites, when the foot motor area was stimulated at the intensity of 20 mA. (B) Both HbO₂ and HbR increased in the hand motor areas when the seizure onset zone was stimulated at an intensity of 16 mA (b and c). In the trunk motor areas (a) and the premotor cortex (d), hemodynamic changes showed a pattern of increased HbO₂ with decreased HbR

associated increase in HbR is thus indicative of higher levels of neural activity and indicates that oxygen consumption exceeds oxygen delivery via the blood supply.

These findings also suggest that stronger stimulations to the brain surface may likely induce increases in both HbO₂ and HbR not only in stimulation sites but also in remote areas that make strong neuronal connections to the stimulation sites. This implies that areas with robust connections are prone to seizure spread, even if remote, and that their connectivity will be reflected in the NIRS data. For instance, in the present study, hand motor cortex exhibited increases in both HbO₂ and HbR upon stimulation of the seizure onset zone. Oxygen consumption exceeded the rate of oxygen delivery, because the two areas had robust connections that lay within one of the epileptic networks. However, in the trunk motor and premotor cortex, which were conceivably not located within main epileptic networks and weakly connected to the seizure onset zone, the rate of oxygen consumption did not exceed the rate of delivery. Further studies are needed to clarify and extend the implications and relevance of such hemodynamic changes in resolving epileptic networks and more weakly connected surrounding areas.

In this study, we employed intraoperative NIRS from four probes to demonstrate that abnormal connectivity between regions of cortex characterizes epileptic network activities. Our results highlight the capability of intraoperative NIRS to provide us with useful information about the dynamics of cortico-cortical activity at high resolution and without artefacts due to scalp blood flow. This approach can thus expand on previous studies using NIRS scalp recordings, such as our description of hemodynamic connectivity between the superior temporal and inferior frontal cortex in the language system. The additional ability to make simultaneous electrical recording would enhance the level of information obtained through this approach. Recently, a thin flexible probe, with a probe head of 5.6×10 mm and the total thickness of 0.7 mm, was developed for simultaneous recording of NIRS and ECoG,^[9] by integrating near-infrared light-emitting diodes and photodiodes for NIRS measurement placed on the brain surface and ECoG electrodes. In their initial experimental study using this novel device, these researchers reported hemodynamic changes associated with both focal brain cooling and hyperventilation. If such small devices

were made widely available and applied in patients undergoing neurosurgery, it could be used to further our understanding of cortico-cortical projections and expand on intraoperative NRIS studies.^[8]

CONCLUSIONS

In a patient with SMA seizures, we employed intraoperative NIRS to demonstrate hemodynamic changes between the SMA, corresponding to the seizure onset zone, and the lateral PMC, corresponding to the seizure propagation areas. This is the first report to report that NIRS can reveal cortico-cortical activities from the brain surface intraoperatively. In the future, intraoperative NIRS will be useful in monitoring cortico-cortical activities such as in the language system and other cortical processes.

ACKNOWLEDGMENTS

This work was supported by JSPS KAKENHI Grant Number 25462246. The authors thank Akihiko Suzuki, Motohiro Soma, and Kiyoe Nonaka for their technical support.

REFERENCES

1. Fukuda M, Masuda H, Honma J, Fujimoto A, Kameyama S, Tanaka R. Ictal SPECT in supplementary motor area seizures. *Neurol Res* 2006;28:845-8.
2. Hatanaka N, Tokuno H, Hamada I, Inase M, Ito Y, Imanishi M, et al. Thalamocortical and intracortical connections of monkey cingulate motor areas. *J Comp Neurol* 2003;462:121-38.
3. Hoshino T, Sakatani K, Katayama Y, Fujiwara N, Murata Y, Kobayashi K, et al. Application of multichannel near-infrared spectroscopic topography to physiological monitoring of the cortex during cortical mapping: Technical case report. *Surg Neurol* 2005;64:272-5.
4. Luppino G, Matelli M, Camarda R, Rizzolatti G. Corticocortical connections of area F3 (SMA-proper) and area F6 (pre-SMA) in the macaque monkey. *J Comp Neurol* 1993;338:114-40.
5. Matsumoto R, Nair DR, LaPresto E, Bingaman W, Shibasaki H, Luders HO. Functional connectivity in human cortical motor system: A cortico-cortical evoked potential study. *Brain* 2007;130:181-97.
6. Morris HH 3rd, Dinner DS, Luders H, Wyllie E, Kramer R. Supplementary motor seizures: Clinical and electroencephalographic findings. *Neurology* 1988;38:1075-82.
7. Sato Y, Fukuda M, Oishi M, Shirasawa A, Fujii Y. Ictal near-infrared spectroscopy and electrocorticography study of supplementary motor area seizures. *J Biomed Opt* 2013;18:76022.
8. Sato Y, Oishi M, Fukuda M, Fujii Y. Hemodynamic and electrophysiological connectivity in the language system: Simultaneous near-infrared spectroscopy and electrocorticography recordings during cortical stimulation. *Brain Lang* 2012;123:64-7.
9. Yamakawa T, Inoue T, He Y, Fujii M, Suzuki M, Niwayama M. Development of an implantable flexible probe for simultaneous near-infrared spectroscopy and electrocorticography. *IEEE Trans Biomed Eng* 2014;61:388-95.