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Exploration of Cerebral Activation using Hemodynamic Modality Separation Method in High-density Multichannel fNIRS

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Abstract—**Hemodynamic modality separation (HMS) is a method for separating the functional near infrared spectroscopy (fNIRS) signal into the cerebral functional and systemic physiological components based on their difference in hemodynamic modalities: 1) Changes in oxyhemoglobin and deoxyhemoglobin (ΔHbO and ΔHbR) in the cerebral capillaries during neural activation negatively correlate with each other; 2) Other physiological hemodynamic changes originating from major vessels cause a positive correlation in ΔHbO and ΔHbR. We applied this simple method to a high-density multichannel (HDM) fNIRS measurement. In the case of functional signal detection in the parietal area of human adults during a single-sided finger-tapping task, conventional fNIRS data showed very unclear signal laterality, while the functional components separated by the HMS method highly localized at the contralateral area of the tapping side. Using the HMS method for HDM NIRS, we successfully explored cerebral activation in the parietal area. This is the first report that HMS method was utilized for the exploratory detection of cerebral activity.**

I. Introduction

Multichannel near-infrared spectroscopy (NIRS) is increasingly utilized to detect changes in the oxygenation and hemodynamics associated with neuronal activation in the cerebral cortex. Many NIRS users consider it to be an easy-to-use technique for exploring the cerebral functional area that is activated by various types of tasks, including a subject's motion. However, most commercially available multichannel NIRS systems are equipped with single-distanced source-detector pairs [1], which are spatially arranged such that channels comprise a lattice with about 30 mm pitch. Therefore, in cases involving the use of such systems for the exploration of the cerebral functional activation area, we encountered two methodological problems. First, the signal obtained by the single-distanced source-detector pair is inevitably contaminated by superficial hemodynamics. Some of these contaminants can be evoked by cognitive tasks [2-4], as well as a subject's motions [5-7], and such contaminants may lead to false positive detections in a much larger area than that originating from the true signal [2-7]. Second, the conventional channel lattice configuration with about 30 mm pitch is too sparse to detect an activated area in the size of a single gyrus [8]. Such sparse sampling leads to a false negative detection by overlooking the activated area. To overcome these problems, we utilized the hemodynamic modality separation (HMS) method combined with a high-density multichannel (HDM) arrangement. In this arrangement, duplicated optode lattices of 30 mm pitch were used and one lattice is placed at the half-pitch shifted position of the other lattice [9]. The HMS method can realize the separation of cerebral functional components from the data obtained with single-distance fNIRS. By combining it with the HDM arrangement, we can obtain a functional mapping with a pitch spatial resolution of 15 mm.

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II. Materials and Method

A. Hemodynamic Modality Separation Method

The details and evaluation of the HMS method were presented in a previous study [10]. Here, we describe it briefly. As we discussed in it, the capillary, which is a major stage of cerebral oxygen delivery, undergoes small changes in the vessel capacity when the cerebral blood flow changes. Hence, simultaneous increases in HbO and decreases in HbR are expected as functional neurovascular hemodynamics in capillary vessels. Other systemic activities such as autonomic nerve regulation and posture changes lead to changes in the capacity of major vessels, in which HbO and HbR may change in the same direction. That is, HbO and HbR in the neurovascular and systemic hemodynamics negatively and positively correlate with each other, respectively. If we assume each correlation to be a linear relationship, the two different signal components can be separated as follows:

$$\begin{pmatrix} \Delta\mathrm{HbO}_\mathrm{F} \\ \Delta\mathrm{HbR}_\mathrm{F} \end{pmatrix} = \frac{1}{k_\mathrm{F} - k_\mathrm{S}} \begin{pmatrix} -k_\mathrm{S} & 1 \\ -k_\mathrm{F} \cdot k_\mathrm{S} & k_\mathrm{F} \end{pmatrix} \begin{pmatrix} \Delta\mathrm{HbO} \\ \Delta\mathrm{HbR} \end{pmatrix} \quad (1)$$

$$\begin{pmatrix} \Delta\mathrm{HbO}_\mathrm{S} \\ \Delta\mathrm{HbR}_\mathrm{S} \end{pmatrix} = \frac{1}{k_\mathrm{F} - k_\mathrm{S}} \begin{pmatrix} k_\mathrm{F} & -1 \\ k_\mathrm{F} \cdot k_\mathrm{S} & -k_\mathrm{S} \end{pmatrix} \begin{pmatrix} \Delta\mathrm{HbO} \\ \Delta\mathrm{HbR} \end{pmatrix}, \quad (2)$$

where the subscript F and S represent the functional and systemic hemodynamic modalities, respectively, and k_M represents a proportional coefficient of the modality M. Because of the difference in the correlation of the two hemodynamic modalities, $k_\mathrm{F} < 0$ and $0 < k_\mathrm{S}$ hold.

Here, we assumed a universal k_F value because the hemodynamics of the neurovascular response can be expected to be universal over the cortex and subjects. Based on past fNIRS studies that observed cerebral functional hemodynamics by using experimental designs to exclude other physiological signals, we set $k_\mathrm{F} = -0.6$ for all channels.

On the other hand, the k_S for each channel may vary with the oxygen saturation level in related vessels. For example, a subject's mental strain often causes an increase in cardiac stroke volume and arterial dilation, whereas a change in the subject's posture causes hyperemia in both arteries and veins. Because these vessels indicate different oxygen saturation

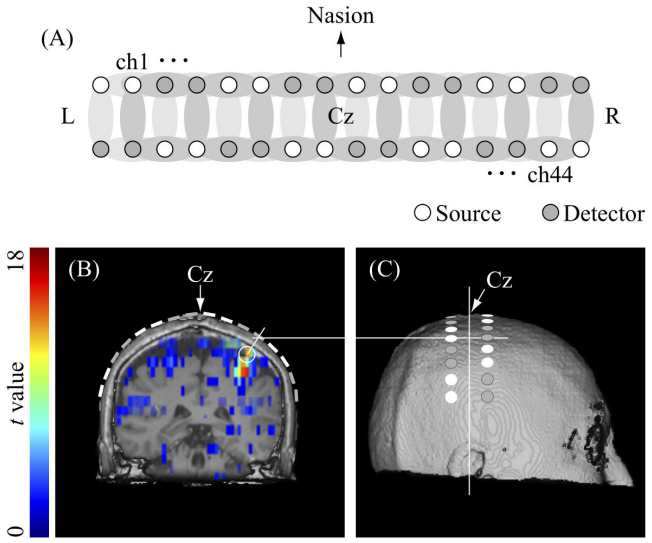

Figure 1. (A) The channel configuration of high-density multidistance NIRS measurement. (B) The fMRI t-contrast image during left finger tapping of participant 1. (C) Optodes position for participant 1.

levels, unlike the case with k_F, we cannot expect k_S to be a universal value for various types of tasks. Nevertheless, two hemodynamic modalities must be caused by different physiological and tissular origins. In such case, high probabilistic independencies of two modalities are expected. Based on this assumption, we made a search for the k_S value which minimizes the mutual information of two hemodynamic components under the condition of k_F = -0.6. The mutual information was calculated as follows:

$$I(k_F = -0.6, k_S) = \sum_{\Delta HbO_F} \sum_{\Delta HbO_S} p(\Delta HbO_F, \Delta HbO_S) \cdot log \frac{p(\Delta HbO_F, \Delta HbO_S)}{p(\Delta HbO_F)\, p(\Delta HbO_S)} \quad , (3)$$

where $p(X)$ represents the probability of X and $p(X, Y)$ represents the joint probability of X and Y. These probabilities were given by histograms of ΔHbO_F and ΔHbR_S, which were calculated based on (1) and (2) with provisionally given k_S.

B. NIRS Channel Configuration and Data Acquisition

The originally designed optodes (16 sources and 16 detectors) and their holder system [11] were used together with a commercially available NIRS measurement system, OMM-3000 (Shimadzu corp., Japan). The channel configuration and position on the subject's head are illustrated in Fig. 1. Duplicated optode lattices of 30mm pitch were arrayed so that one lattice is placed at 15 mm shifted position of the other, which comprise 44 channels. The center of the optode array was placed at the Cz position of the EEG 10-20 method so that the region of the HDM measurement covered the primary motor area of participants. For participant 1, the primary motor area was initially identified by functional magnetic resonance imaging (fMRI) using the task design described below [6].

TABLE I. NUMBER OF CHANNELS INDICATING STATISTICAL SIGNIFICANCE IN PAIRED T-TEST

Participants	ΔHbO		ΔHbR		ΔHbO_F	
	L-hem.	*R-hem.*	*L-hem.*	*R-hem.*	*L-hem.*	*R-hem.*
P1	0	5	3	2	7	7
P2	0	6	0	11	0	9
P3	0	0	0	0	1	1

Data were sampled at intervals of 130 ms. Hemoglobin data obtained by the system was used as ΔHbO and ΔHbR in (1) and (2). Using various k_S in the range $0 < k_S < 1$, we calculated the mutual information $I(k_F = -0.6, k_S)$ in (3), and found the $\Delta HbO_F/\Delta HbR_F$ and $\Delta HbO_S/\Delta HbR_S$ that minimize $I(k_F = -0.6, k_S)$.

C. Task Design and Statistical Analysis

Three healthy adult volunteers participated in the experiment. Each participant was in a seated position and was instructed to perform the following task sequence: tap the left finger (20 s), rest (20 s), tap the right finger (20 s), and rest (20 s). After the preceding rest period (20 s), this sequence was repeated five times. In the tapping task, a thumb was tapped with the index finger in the single-side hand at a frequency of 4 Hz.

For the statistical analysis to detect the cerebral activity, a paired t-test for the difference in the hemoglobin change between the tasks was conducted using the following procedure. Hemoglobin changed during the tasks and their preceding rest periods (each with a duration of 10 s) were averaged, where a temporal offset of 10 s in each period was considered as the transient phase of the functional hemodynamics. The difference between the task and the preceding rest was averaged for five trials of each tapping side. For the results, the difference between the tasks of the left and right finger tappings was examined by the paired t-test.

This study was approved by the Institutional Review Board of AIST. Written informed consent was obtained from each participant.

III. RESULTS AND DISCUSSION

Fig. 2A shows temporal changes in the conventional fNIRS data (ΔHbO and ΔHbR) of participant 1, and Fig. 2B shows those in the functional components obtained by the HMS method (ΔHbO_F and ΔHbR_F). All the data were block averaged. Asterisked frames on both lateral sides in each figure indicate the positions directly above the activation area in which the highest t-contrast was observed in the fMRI experiment. Thick frames represent channels in which the statistical significance in the oxyhemoglobin difference between left and right finger tapping was obtained (gray, $p < 0.05$; black, $p < 0.01$).

In Fig. 2A, the ΔHbO increase was evoked by task execution in most channels. This may be because changes in the cardiac stroke volume and arterial dilation by autonomic

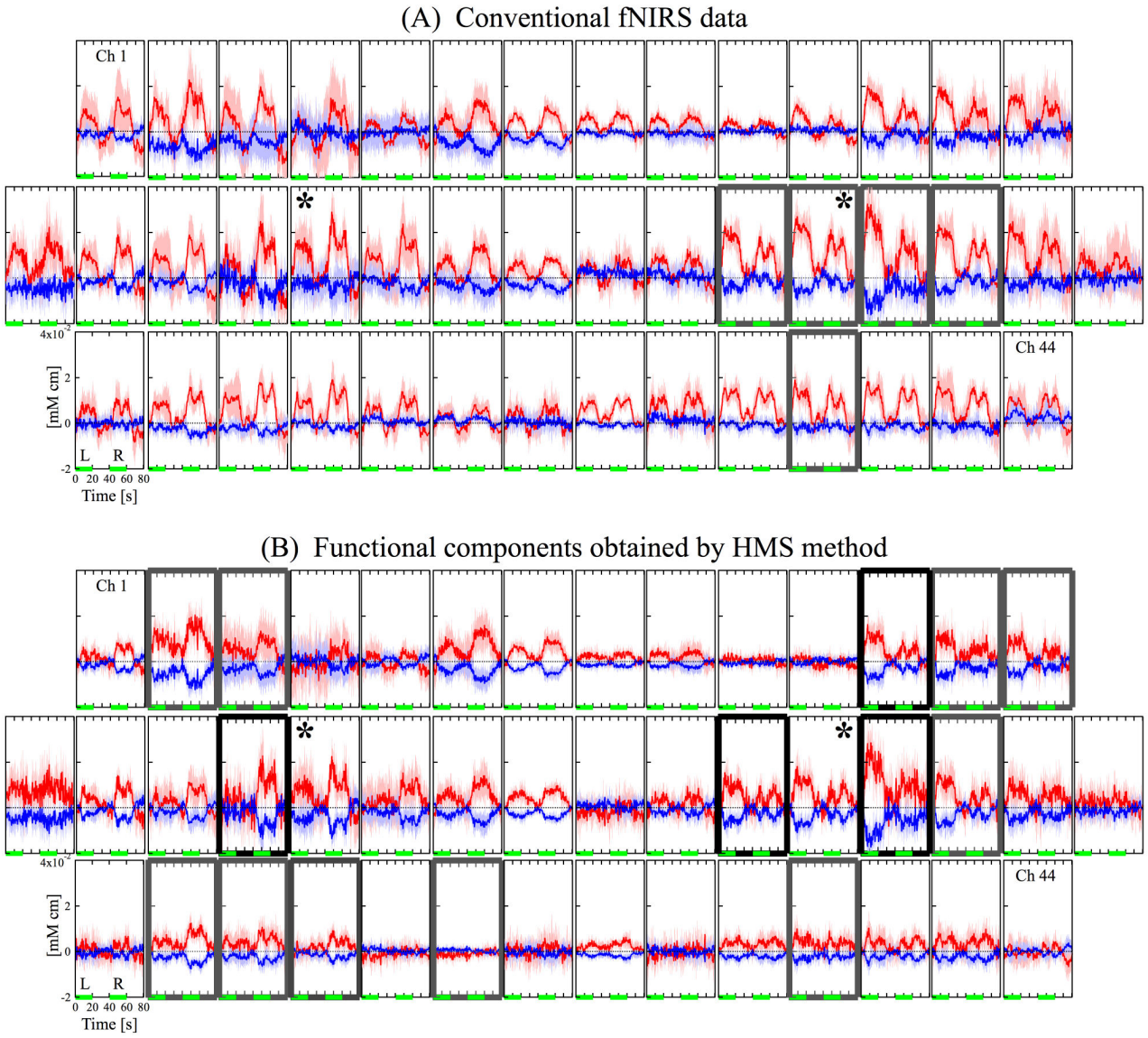

Figure 2. Cerebral functional signal detection for participant 1 obtained using high-density multicannel optode configuration. (A) Conventional fNIRS data, ΔHbO and ΔHbR. (B) Functional components onbtained by the hemodynamic modality separation method, ΔHbOF and ΔHbRF. Red and blue lines indicate block-averaged changes in oxyhemoglobin and deoxyhemoglobin, respectively. The standard deviation of each change was shown as a band having the same color. Green lines indicate the period of task execution. Channels that indicate the statistical significance of $p < 0.05$ and $p < 0.01$ in the difference between left and right finger tapping were framed by thick gray and black lines, respectively. The asterisked channel in each side corresponds to the position directly above the activation area identified by the fMRI measurement.

nerve regulation were induced by task execution. Accordingly, the laterality in the ΔHbO increase caused by left and right tapping was very unclear. Moreover, the channels indicating $p < 0.05$ were not symmetrically lateralized. No channel indicated $p < 0.01$.

In Fig. 2B, the ΔHbO_F changes in most channels were smaller than those of ΔHbO (Fig. 2A). In particular, the increases due to both task executions were effectively reduced in peripheral channels. On the other hand, the differences in laterality at several channels were more clearly observed. Consequently, ΔHbO_F showed significant symmetrical laterality. This may be because fluctuations that were due to systemic hemodynamics could be effectively separated from ΔHbO_F. The channels indicating the statistical significance were concentrated in the position directly above the activated area (asterisked frames) on both sides.

The statistical analysis for three participants is shown in Table I, which summarizes the number of channels, indicating the difference of $p < 0.05$ by the tapping side in ΔHbO, ΔHbR, and ΔHbO_F at each hemisphere. The numbers for ΔHbO and ΔHbR showed low symmetry in laterality, whereas the numbers for ΔHbO_F showed high symmetry in laterality in most cases. However, in the case of participant 2, sufficient lateral symmetry was not shown, even in the numbers for ΔHbO_F. Actually, in this case, a channel around C3 and C4 positions, which respectively corresponds to the positions above the left and right primary motor areas [12], showed a symmetrical difference in the amplitude of ΔHbO_F (data not shown). However, a larger noise was observed only

in the channel around C3, and this unfavorable noise condition caused a lower t-value than that caused around counter-side channels.

The noise condition varies primarily with the hair covering the optodes at the channel; thus, the noise variance in the data inevitably differs in each channel. In addition, the signal amplitude in the NIRS measurement is scaled differently with the optical path length at each channel, and the path length considerably varied with the position of channel [13]; hence, the signal amplitude at a given channel cannot be directly compared with that of other channels. For these reasons, the statistics in fNIRS signals may sometimes lead to different results from the t-contrast image obtained by fMRI. Even in the case of participant 1, by carefully reviewing Fig. 2B, we note that the most significant point in each hemisphere did not necessarily coincide with that of the fMRI measurement. To address this problem, some statistical procedure for multiple comparisons that consider differences in the noise and scaling conditions over channels will be required. This is a further issue that needs to be addressed to realize a more accurate mapping of cerebral activity using fNIRS. In this study, instead of such a precise approach, we simply applied the paired t-test between the target and the reference tasks for each channel. It revealed that a more reliable exploration of the cerebral activation area than the conventional detection could be realized using the HMS method.

IV. Conclusion

The fNIRS is an easy-to-use technique compared to other neuroimaging techniques such as fMRI and PET. In particular, the HMS method has advantages compared to other NIRS methods for the detection of cerebral activity. This method is applicable to the single-distance detection of the continuous wave NIRS technique, which requires no further high-specification devices, such as detectors of larger dynamic range, short pulse lasers, and time-amplitude converters, and or extremely complicated configurations in the optode array. Moreover, unlike the tomographic technique, this method does not require a large amount of calculation for the exploration of the cerebral activation area because of its simple algorithm, which enables us to directly implement it, even on commercially available NIRS systems. By simultaneously using the HMS method with HDM measurement, the users of the existing systems can increase reliability in the exploration of cerebral functional activity in a less expensive and simple way.

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