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Near-Infrared Spectroscopy and Motor Lateralization after Stroke: A Case Series Study

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Abstract

Near-infrared spectroscopy (NIRS), which allows non-invasive monitoring of cerebral activation, might be a useful tool to assess brain activity in stroke patients because it allows recording without imposing restraints on the subject's posture. Previous NIRS studies on stroke patients have focused on brain activation in patients with mild impairment or full recovery, and there has been a lack of data on patients without recovery. In the present study, we compared the hand movement-related brain activation pattern and laterality balance of healthy subjects and of stroke patients with mild or moderate hemiparesis in the chronic phase. In normal subjects, predominantly contralateral activation was observed during unilateral hand grasping. Similar contralateral-predominant activation was observed during grasping with the unaffected hand in stroke patients, and during affected-hand grasping in patients with mild hemiparesis. However, abnormal activation patterns, i.e., bilaterally increased activation and ipsilateral-predominant activation, were observed during affected-hand grasping in patients with moderate hemiparesis. These findings suggest that differences in brain activation patterns in stroke patients are well detected by NIRS.

Key words:

fNIRS; Reorganization; Laterality; Rehabilitation; Stroke; Hemiparesis

Introduction

Hemiparesis and hemiplegia are the most common disorders after stroke. Motor functional recovery from the neurological deficit can occur, but the extent of recovery varies widely [1]. Previous studies using functional magnetic resonance imaging (fMRI), positron emission tomography, and electroencephalography demonstrated that abnormal activation patterns in motor-related areas, such as the primary sensorimotor cortex (SM1), premotor cortex (PM), supplementary motor areas (SMA), and the cerebellum, could be seen during unilateral finger or hand movement in stroke patients [2-9]. During affected-hand movement, motor-related activations in the hemisphere ipsilateral to the moving hand are often observed [10,11].

The activations in the ipsilateral motor network cause a change in lateralization balance from normal contralateral to abnormal bilateral- or ipsilateral-predominant laterality. In addition, a reallocation back from the abnormal control to normal contralateral control may play an important role in good functional recovery [11]. Intra- and inter hemispheric interactions during voluntary hand movement were assessed with fMRI and dynamic causal modeling [12]. The functional connectivity studies suggested that a dysfunction of the connectivity between both sides of primary motor cortex underlies hemiparesis after stroke [13], and a reinstatement of functional connectivity between PM and ipsilesional (contralateral to the moving hand) primary motor cortex is an important feature of motor recovery [14].

Near-infrared spectroscopy (NIRS), which uses near-infrared light to measure the change in concentrations of oxygenated and deoxygenated hemoglobin (Δ[Oxy-Hb] and Δ[Deoxy-Hb], respectively. The capital letter delta and brackets stand for "change" and "concentration", respectively.) in response to neural activation [15], is a non-invasive brain imaging technique. Since, NIRS generally allows recording without imposing too many constraints on the subject's posture, as other techniques do, it may be the most convenient technique for stroke rehabilitation and recovery studies [16-18]. Moreover, activations in the premotor cortex during application of several stroke rehabilitation methods [19] and in motor-related areas during hemiparetic gait [20-22] have been reported. Cerebral activations during hemiparetic hand movement have also been assessed using NIRS. Using both NIRS and fMRI, we have shown a contribution of ipsilateral motor areas to hemiparetic hand movement [23]. In two earlier studies using laterality index, including ours [24,25], the lateralization change from ipsilateral or bilateral to the contralateral hemisphere was accompanied by motor functional recovery. However, these previous studies mainly focused on well or fully recovered hemiparetic stroke patients.

In the present study, therefore, we used NIRS to record hand grasp-related activation in motor-related brain areas in 10 stroke patients who had persistent mild or moderate hemiparesis in the chronic phase (>3 months), and examined the relationship between cerebral laterality balance and degree of paralysis to further establish the usefulness of NIRS in the assessment of brain activation in stroke patients.

Materials and Methods

Subjects

Ten first-ever stroke patients (61 ± 11 years old; 7 females and 3 males; Table 1) who suffered from hemiparesis after stroke in the thalamus or putamen were recruited at the chronic phase. Five of the patients (Patient No. 2, 4, 5, 7 and 8) were in the hospital receiving regular physical and occupational therapies approximately every day. The other patients (Patient No. 1, 3, 6, 9 and 10) were provided the same rehabilitation therapy for once or twice a week. The locations of cerebral infarction or hemorrhage were demonstrated by MRI or CT (Figure 1). All the patients were right-handed and could move their affected hand. We used the Brunnstrom stage (Br. Stage) for the hand [26] to evaluate the motor dysfunction and classified the patients into 2 groups as having moderate hemiparesis (Br. Stage 3-5, Patients No. 1-6) and mild hemiparesis (Br. Stage 6 or normal, Patients No. 7-10). Eight right-handed normal subjects (52 ± 13 years old; 5 females and 3 males) served as controls. Handedness was evaluated using the Edinburgh inventory [27]. NIRS recordings were made after obtaining informed consent from all the subjects according to the Declaration of Helsinki. The present study was approved by the ethics committee of the International University of Health and Welfare.

Patient No.; age; sex; handedness	Location; Stroke type	Affected hand; Br. Stage	Time science stroke [Months]
1; 65; F; R	L putamen; hemorrhage	R; III	16
2; 80; F; R	R putamen; infarction	L; IV	3
3; 61; M; R	R putamen; infarction	L; IV	67
4; 42; M; R	R putamen; hemorrhage	L; IV	4
5; 60; M; R	L putamen; infarction	R; IV	4
6; 56; F; R	R putamen; hemorrhage	L; V	54
7; 73; F; R	L putamen; infarction	R; VI	3
8; 72; F; R	R thalamus; hemorrhage	L; VI	3
9; 53; F; R	R putamen; infarction	L; n	19
10; 52; F; R	L thalamus; infarction	R; n	8

Table 1: Characteristics of Patients. Brunnstrom Stage (Br. Stage)

I: No muscle tone can be sensed.

II: Little or no active finger flexion. Presence of muscle spasticity.

III: Mass grasp or hook grasp. No voluntary finger extension or release.

IV: Semi-voluntary finger extension in a small range of motion.

V: Cylindrical and spherical grasp. Voluntary mass finger extension.

VI: Near normal. Voluntary finger extension (full range of motion)

n: Normal

Motor paradigm

During the NIRS recordings, an auditory metronome (60 beats/min) was played through a speaker placed behind the subject. While sitting in a comfortable chair with their eyes closed, the subjects performed a unilateral voluntary hand-grasping task in synchrony to the beat. Subjects performed the following sequence five times: a 15 s resting block (baseline); a 15 s block with right hand grasping; a 30 s resting block; a 15 s block with left hand grasping; and a 15 s resting block. We video recorded the patients and confirmed visually that no patient had associated movements or mirror hand movements. The motor paradigm was the same as previously described [25].

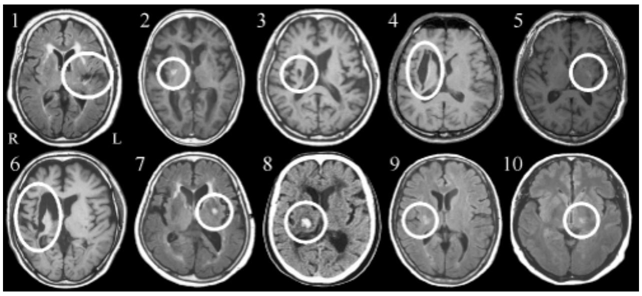

Figure 1: Locations of cerebral infarction or hemorrhage (white circles), imaged by MRI (cases 1-7, 9, and 10), or CT (case 8).

NIRS recordings

NIRS recordings during the task were performed using an optical topography system (ETG-4000; Hitachi Medical, Tokyo, Japan). Eight light-emission and seven light-detection probes were arranged in a 3×5 rectangular lattice and were placed 3 cm apart from each other to produce 22 recording channels. Two of these lattices were placed onto the scalp overlying the SM1 and PM of both cerebral hemispheres. Because the C3 and C4 points of the international 10-20 system for EEG are thought to be located over the left and right pre- and postcentral gyri (primary sensorimotor cortex, associated with voluntary movement) [28,29], these points were specially assigned to channels 11 and 34, respectively (Figure 2).

NIRS data analyses

NIRS data analyses were performed as described previously [25] with slight modifications. Two near-infrared laser beams (wavelengths at 695 and 830 nm) were emitted and reflectance beams sampled at 10 Hz were used to calculate Δ[Oxy-Hb] and Δ[Deoxy-Hb]. The changes in the Hb concentrations were detrended, smoothed with a 3 s moving average, and averaged across the five grasping blocks for each hand. We focused on Δ[Oxy-Hb] because it is the most sensitive marker of Hb concentration changes [28-30].

Standard deviation (SD) of the Δ[Oxy-Hb] for each channel was calculated against 10 s resting periods just before the grasping blocks, and the z score for each channel was calculated by dividing the mean amplitude of the hemodynamic signal in the interval 5-15 s after the onset of the grasping blocks by the SD. A color image (z map) of each hemisphere was generated using a cubic spline interpolation of the z scores of 22 channels. A response was deemed significant when the z score was above 3.053, which is the one-sided Bonferroni-corrected significance level of multiple comparisons for 44 channels [25]. The

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ratio of the area with significant activation to the whole recording area (the extent ratio) was calculated for each hemisphere, and was compared among six groups, i.e., (1) right hand grasping by normal subjects, (2) left hand grasping by normal subjects, (3) affected-hand grasping by moderately hemiparetic patients, (4) unaffected-hand grasping by moderately hemiparetic patients, (5) affected-hand grasping by mildly hemiparetic patients, and (6) unaffected-hand grasping by mildly hemiparetic patients.

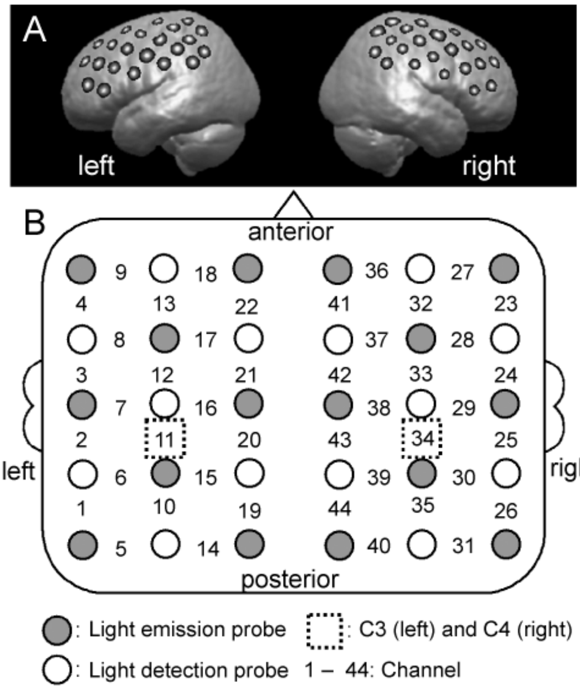

Figure 2: A: Locations of the recording channels of the present NIRS study. B: Location of NIRS probes. Channels 11 and 34 were placed onto the C3 and C4 points, respectively. The length axis of each head shell was parallel to the nasion-inion line.

To determine which cerebral hemisphere was predominantly activated during hand grasping, we defined a contralaterality index (CI) as CI = (Rc-Ri)/(Rc+Ri), where Rc and Ri denote the ratio of activation (percentage of the recording area) in the contralateral and ipsilateral hemispheres, respectively. The CI ranges from -1 (exclusively ipsilateral activation) to +1 (exclusively contralateral activation).

These signal processing, z score calculation, and z map creation were performed using Matlab 2007b (MathWorks, Natick, MA, USA).

Results

All the stroke patients were able to perform the task adequately, and did not show head movements or mirror movements during the NIRS recordings. We observed a significant task-related increase in Δ[Oxy-Hb], and a concomitant decrease or no change in Δ[Deoxy-Hb] in each hemisphere in all the subjects.

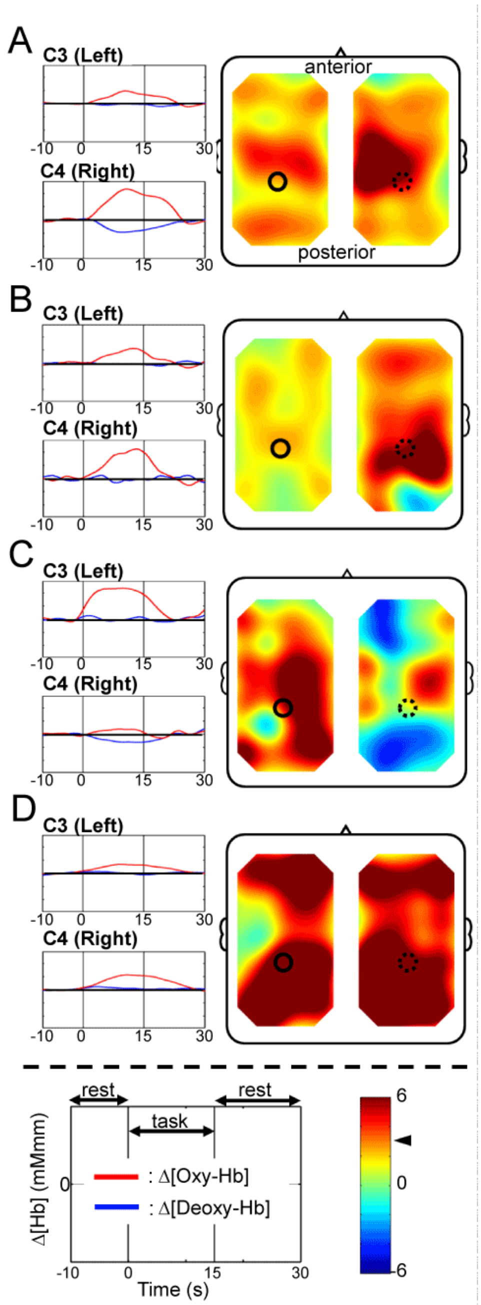

Figure 3: NIRS topography (z map), and Δ[Hb] (red, Δ[Oxy-Hb]; blue, Δ[Deoxy-Hb]) in channels 11 (C3) and 34 (C4) during left hand grasping (affected hand in stroke patients). These channels are over the left and right sensorimotor cortex, which is closely associated with voluntary movement. A: contralateral-predominant pattern in normal subjects. B: contralateral-predominance in a patient with mild hemiparesis (Patient No.9). C: ipsilateral-predominance in a patient with moderate hemiparesis (Patient No. 2). D: bilateral activation in a patient with moderate hemiparesis (Patient No.3). Arrowhead: significance level of the topography.

Figure 3 shows topographic color images obtained by spatially plotting the z scores, and the time courses recorded at the C3 and C4

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points during left hand grasping (affected-hand grasping in stroke patients). Normal subjects and stroke patients displayed a contralateral-predominant activation pattern during normal (Figure 3A) and unaffected hand grasping. Patients with mild hemiparesis also showed the contralateral-predominant activation pattern (Figure 3B). The patients with moderate hemiparesis showed two patterns of activation, ipsilateral-predominant activation (Figure 3C) and bilaterally increased activation (Figure 3D) during affected-hand grasping.

The extent ratios in each hemisphere of each participant are shown in Figure 4. There was no essential difference between right and left hand movements in normal subjects. Except for affected-hand grasping in patients with moderate hemiparesis, the activation in the contralateral hemisphere was more extensive than that in the ipsilateral hemisphere. All the patients with moderate hemiparesis tended to show widespread ipsilateral activation during affected-hand grasping. Three of the patients with moderate hemiparesis (Patients No. 3, 4, and 6; Figure 4, filled squares) also showed widespread activation in the contralateral hemisphere (bilaterally increased activation) during affected-hand grasping, whereas the other three patients (Patients No. 1, 2, and 5; filled triangles) showed low contralateral activation (ipsilateral-predominant activation).

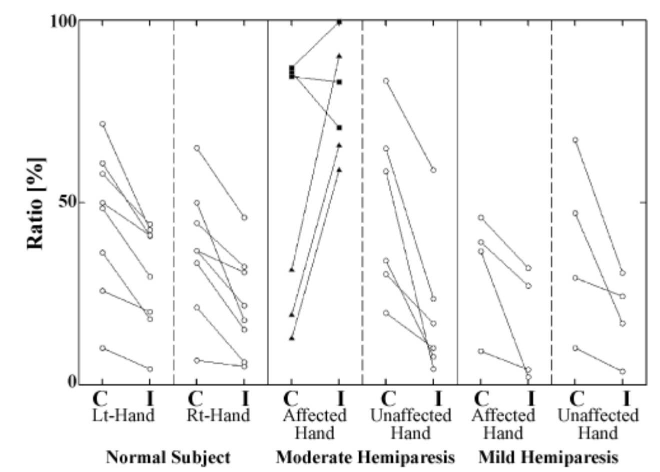

Figure 4: The ratio of the cerebral cortex area with significant activation to that of the entire imaged portion of the hemisphere (the extent ratio) of all subjects. During normal hand grasping of healthy subjects and unaffected-hand grasping of patients, the contralateral hemisphere was predominantly activated. In contrast, the ipsilateral hemisphere was extensively activated during moderately paretic hand grasping. C, contralateral hemisphere; I, ipsilateral hemisphere; Lt, left; Rt, right; Filled squares, patients with bilateral activation; Filled triangles, patients with ipsilateral-predominant activation.

The CIs for each group are shown in Figure 5. The contralateral-predominant CI was observed during normal subjects' hand grasping and unaffected-hand grasping in all the stroke patients. The patients with mild hemiparesis also showed the contralateral-predominant pattern for the affected hand, while those with moderate hemiparesis showed lower CIs than unaffected-hand.

Discussion

The advantages of NIRS are its relatively low restraint on the subjects and its insensitivity to motion artifacts during recording [18]. The cerebral activity of stroke patients who cannot tolerate the restraint needed for fMRI or PET scans can be measured by NIRS without difficulty. Previous NIRS studies, which assessed the activation during affected-hand movement of mild hemiparetic patients, reported that NIRS could yield activation measurements similar to those of other non-invasive brain imaging techniques [23-25]. Since there was a lack of data on patients with persistent moderate hemiparesis, we recruited such hemiparetic patients together with mild hemiparetic patients. The laterality difference which depends on the degree of the paralysis of the affected hand could be successfully detected. The simplicity and safety in clinical application of NIRS may enable us to assess easily the effect of clinical practice. In fact, Mehnert et al. used NIRS to examine the effect of mirror therapy on the hemispheric lateralization [31], which had previously been reported using fMRI [32,33].

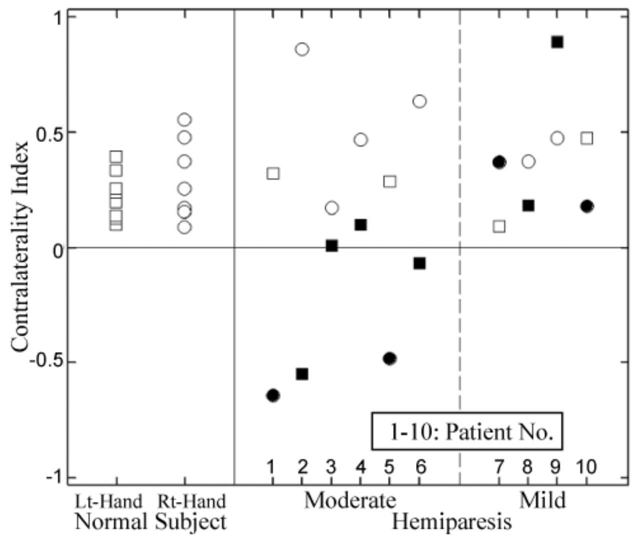

Figure 5: Contralaterality indices (CIs) of all the subjects. All the CIs for normal subjects and for unaffected-hand grasping of the patients were above 0, which indicates contralateral-predominant activation. CIs for moderately paretic hand grasping were classified into 2 groups, i.e., three patients with bilateral activation (CIs were around 0; Patients No. 3, 4, and 6) and ipsilateral-predominant activation (CIs were below 0; Patients No. 1, 2, and 5). Squares, left hand grasping; Circles, right hand grasping; Filled symbols, affected-hand grasping.

Laterality index is one of the approaches for evaluating the hemispheric balance. NIRS signals include an uncertain parameter [34,35], optical path length, which mainly depends on the thickness of the scalp surface or the thickness of the cerebrospinal fluid layer and it is not correct to use the height of amplitude directly. Therefore, we did not use the amplitude of Δ[Hb] directly as a marker to calculate the index in the present study. We calculated a statistical parameter, z score, during the task against baseline to make the topography map for an alternative measure, and the extent of significant activation was used to assess the hemispheric balance. The laterality comparison based on the extent of activation could successfully detect the contralateral-predominant activation pattern during the normal hand grasping of healthy subjects and during unaffected-hand grasping in stroke patients, and during affected-hand grasping in patients with mild hemiparesis.

In this NIRS study, the task-related increases in Δ[Oxy-Hb] and the concomitant decreases in Δ[Deoxy-Hb] were observed mainly in the contralateral hemisphere during grasping by the normal subject, by the unaffected hand of all the patients, and by the affected hand of mild hemiparetic patients. These are typical time courses in NIRS recording. However, increases in Δ[Oxy-Hb] appeared bilaterally causing a reduction in the contralaterality, in contrast to the clearer contralateral-dominant activations that could be seen in previous fMRI studies during unilateral hand movement [23,36]. Previous NIRS studies [25,31] also showed an increase in Δ[Oxy-Hb] in the ipsilateral hemisphere which is not clearly mentioned. Recent reports have cautioned that scalp blood flow, which shows a systematic task-related change, contaminates the NIRS signals [37,38]. The scalp blood flow artifact may generally be one of the reasons for the lower contralaterality seen in NIRS studies. For the same reason, we did not try to divide the activation areas into SM1, PM, and SMA. Development of methods to remove the artifact will permit functional-anatomic specification of the activation areas as in fMRI studies [2,3,5,39]

For mild hemiparetic patients, our previous longitudinal NIRS study [25] showed that motor functional recovery was accompanied by a shift of motor activation from bilateral brain activation, which was caused by an addition of ipsilateral control, to contralateral-predominant activation in SM1. The shift was observed at one month after stroke. In the present study, we also observed a clear contralateral predominant pattern in the mild hemiparetic patients at chronic phase. These findings are generally in accord with previous neuroimaging studies [3,8,9], which suggested that motor functional recovery after stroke is associated with restoration of the laterality balance of motor-related activation. The present findings also suggest that the brain recruits the surviving motor system during motor functional recovery, and that the best recovery is obtained when the original motor system is reusable.

Abnormal bilateral and ipsilateral predominant patterns were observed in the moderate hemiparetic patients. The activation in the contralateral hemisphere seems to be divided into 2 groups: strong and weak contralateral activations. Rehme et al. [14] showed that the reinstatement of connectivity in the contralateral (ipsilesional) hemisphere is important for motor recovery. Another fMRI study also suggested that increasing contralateral M1 activity predicts the functional recovery after stroke [40]. Therefore, the extent of the contralateral activation provided by NIRS may have a potential to assess the prognosis for motor function in stroke patients. On the other hand, widespread activation was observed in the ipsilateral hemisphere of all of the moderate hemiparetic patients. The extent seems to be wider than that in normal subjects or mild hemiparetic patients. The contribution of the ipsilateral hemisphere to the motor recovery is controversial divided into supportive and inhibitory roles. However, the ipsilateral hyperactivation causes the reduction of contralaterality and could be useful to detect the abnormality of cerebral activation of stroke patients.

The generalizability of our results has limitations because the sample size is not large enough compared with most fMRI study. Our samples had different time points from stroke onset (3-67 months), ages (42-80 years old), stroke types, and stroke sides. Especially, the time from stroke onset is the most important factor of the motor functional recovery. Hendricks et al. reported that motor functional recovery will be plateau after 6 months after the stroke onset [41]. This study, however, has a wide range of the time after stroke onset. Although ages at onset of stroke [42] and stroke side [43] have also been considered as key factors of reorganization after stroke, these two factors cannot be reported in this study because of our small patients sample size. However, differences in laterality balance during unilateral hand movement among normal subjects and mildly and moderately hemiparetic patients could be detected with NIRS in the present study. Therefore, we conclude that NIRS is a useful tool for monitoring brain activation and the assessment of laterality in stroke patients.

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