Effects of Revascularisation on Evoked Cerebral Blood Oxygenation Responses in Stroke Patients

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Abstract We demonstrated that ischemic strokes exhibit an increase of deoxyhemoglobin during activation. We evaluated the effect of revascu-larization on the abnormal evoked cerebral blood oxygenation (CBO) re-sponses in these patients, employing near-infrared spectroscopy (NIRS). We selected five patients who exhibited an increase of deoxyhemoglobin associated with increases of oxyhemoglobin and total hemoglobin during activation for this study. These patients showed marked reductions of base-line regional cerebral blood flow and cerebrovascular reserve capacity, which were improved 1 week after revascularization. Postoperative NIRS demonstrated that the increase of deoxyhemoglobin during activa-tion was not observed after revascularization. This preliminary study demonstrated that the abnormal evoked-CBO response in ischemic stroke patients could be improved by revascularization.

1 Introduction

Blood oxygenation level-dependent (BOLD) contrast functional MRI (BOLD-fMRI) has been used in functional studies on stroke patients, on the assumption that these patients have normal neurovascular coupling [1–3]. Recent studies have revealed, however, that BOLD-fMRI does not correctly image activation areas in stroke patients [4–10]. It was suggested that impairments of neurovascular coupling may alter the evoked cerebral blood oxygenation (CBO) responses and hemodynamic changes in stroke patients, and this could result in failure of BOLD imag-ing. BOLD-fMRI alone, however, cannot elucidate the precise mechanisms involved, since BOLD-fMRI provides information mainly about concentration changes of deoxyhemoglobin (deoxy-Hb), which is paramagnetic [11].

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Recently, we have evaluated evoked CBO changes in the primary sen-sorimotor cortex (PSMC) of patients with ischemic stroke [12, 13], employing near-infrared spectroscopy (NIRS) which allows measurements of concentration changes of not only deoxy-Hb, but also oxyhemoglobin (oxy-Hb) [14]. NIRS demonstrated a decrease of deoxy-Hb with in-creases of oxy-Hb and total hemoglobin (= sum of deoxy-Hb and oxy-Hb, t-Hb) in the activated PSMC on the non-lesion side, which is consistent with the physiological basis of BOLD imaging [11]. However, in the PSMC on the lesion side, the concentration of deoxy-Hb increased during the entire course of activation, concomitantly with increases of oxy-Hb and t-Hb. In addition, BOLD-fMRI showed significantly smaller activa-tion volumes in the PSMC on the lesion side. These findings suggest that the increase of paramagnetic deoxy-Hb during activation caused a reduction of BOLD signal, and this resulted in the failure of BOLD imaging in stroke patients [14].

We hypothesized that the abnormal evoked CBO response was caused by decreases of baseline CBF and cerebrovascular response (CVR) in ischemic stroke patients. In order to test this hypothesis, we evaluated the effects of revascularization on the evoked CBO changes in ischemic strokes.

2 Methods

We studied 5 patients with cerebral ischemia (four males, one female, 65.6 $\pm$ 10.6 years). All of the patients had suffered hemodynamic compromise caused by occlusion of the internal carotid artery (ICA) in four cases and stenosis of the ICA in one case. Four patients received superficial temporal artery-middle cerebral artery (STA-MCA) anastomosis, while one patient received carotid endarterectomy (CEA). The patients did not show neurological deficits at the time of examination.

We evaluated the rCBF at rest and the %CVR response to acetazolamide (1.0 g; ACZ) in the territory of the MCA, employing single photon emission tomography (SPECT) (PRISM 2000XP, Shimadzu Co., Japan): %CVR = {(rCBFACZ-rCBFrest)/rCBFrest} $\times$ 100, where rCBFACZ and rCBFrest represent the rCBF before and after the injection of ACZ, respectively.

We measured the evoked CBO responses in the PSMC contralateral to the task performance using a multi-channel NIRS (OMM 2000, Shimadzu Co., Japan). This system consists of 16 light-source fibers and 16 detectors, resulting in 48 source-detector pairs; each light source has three laser diodes with wavelengths of 780, 805, and 830 nm [15, 16]. The optodes for the NIRS topography were placed on the skull to cover the the motor cortex, employing a holder cap to avoid motion-related artifacts; the distance between each optode was 30 mm. We measured the concentration changes in oxy-Hb, deoxy-Hb, and t-Hb in the PSMC on the lesion side during contralateral hand-grasping tasks. The task paradigm consisted of 40 s of rest and 40 s of self-paced hand grasping; this task-rest cycle was repeated 6 times.

We evaluated the changes in oxy-Hb, deoxy-Hb, and t-Hb by subtracting the mean baseline values (40 s) from the mean stimulation values (40 s). Comparisons were made for each of the NIRS parameters using paired *t*-tests ($p < 0.05$ was defined as the criterion of a significant difference).

We classified NIRS responses into three patterns depending on concentration changes of deoxy-Hb during activation. That is, the deoxy-Hb concentration significantly decreased (Pattern 1), did not change (Pattern 2), or significantly increased (Pattern 3). Both oxy-Hb and t-Hb increased during the task in all subjects.

3 Results

Figure 1 shows an example of evoked CBO changes before and after revascularization. Note that revascularization reversed the direction of deoxy-Hb changes, and increased the extent of the increases in oxy-Hb and t-Hb. Preoperative NIRS demonstrated an increase of deoxy-Hb associated with increases of oxy-Hb and t-Hb (Pattern 3) during activation in all patients,

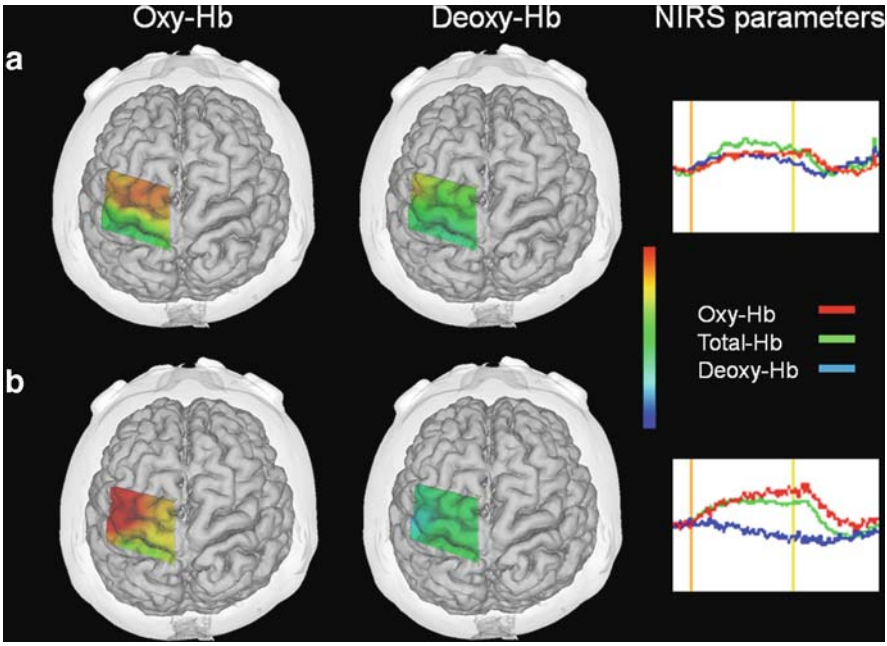

Fig. 1 NIRS topographic maps of changes in oxy-Hb and deoxy-Hb during right grasping task overlaid on anatomical MRI surface images before (**a**) and after (**b**) revascularization. The cir-cles indicate the ROI for analysis of NIRS parameter changes (*right*). Note that revascu-larization reversed the direction of deoxy-Hb changes, and increased the extent of the increases in oxy-Hb and t-Hb

while postoperative NIRS demonstrated a decrease of deoxy-Hb (Pattern 1) in three patients and no change of deoxy-Hb (Pattern 2) in two subjects.

Preoperative SPECT showed reductions of baseline rCBF and CVR in all patients; the mean rCBF and CVR were 40.9 ± 6.4 ml/100 g/min and –23.1 ± 5.6%, respectively. After revascularization, the rCBF and CVR were increased to 45.5 ± 6.1 ml/100 g/min and –5.6 ± 9.6% ($p < 0.016$), respectively.

4 Discussion

A number of studies have shown that revascularization improves the baseline rCBF and CVR in ischemic stroke patients [17–19]; however, until now, there has been no study to evaluate the effect of revascularization on the evoked CBO changes in ischemic stroke patients. The present study demonstrated that the abnormal evoked CBO response (i.e. an increase of deoxy-Hb during activation) in ischemic stroke patients could be improved by revascularization, and the improvement was associated with increases of baseline rCBF and CVR.

It should be noted that improvements of the abnormal evoked CBO response required only 1 week after revascularization. This suggests that the abnormal evoked CBO response was not caused by structural changes of cerebral vessels, such as decreases of elasticity and compliance of the vessels due to arteriosclerosis. Therefore, we considered the physiological mechanism of the deoxy-Hb increase during activation from the viewpoints of hemodynamic effects and oxygen metabolism. That is, the reduction of the rCBF and CVR under resting conditions could cause a lesser rCBF increase during activation, resulting in a decrease of the driving force to wash out deoxy-Hb in the capillaries and veins. When such an impairment of the hemodynamic response is advanced, the oxygen extraction could increase due to a decrease of oxygen delivery during activation. These alterations in the hemodynamic effects and the oxygen metabolism could lead to a lesser decrease or elevation of the deoxy-Hb concentrations in the vessels.

The increase of deoxy-Hb during activation suggests the occurrence of relative ischemia at the activation areas. Quantitative models of oxygen delivery during activation predict that disproportionately large increases of rCBF are required for small increases of the oxygen consumption [20]. Thus, a small decrease in the evoked rCBF response can cause oxygen deficiency during activation. These observations suggest that the relative ischemia during activation contributes to the occurrence of ischemic events. Further studies are necessary to investigate the relation between evoked CBO response patterns and ischemic events.

5 Conclusion

The baseline cerebral ischemic condition affects the evoked CBO response pattern in ischemic stroke patients. The abnormal CBO response in ischemic stroke patients could be normalized by revascularization. The improvements of the

abnormal evoked CBO response required only 1 week after revascularization, suggesting that the abnormal evoked CBO response was due to hemodynamic effects, rather than structural changes of cerebral vessels caused by arteriosclerosis.

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