

SHORT REPORT

Increase in focal concentration of deoxyhaemoglobin during neuronal activity in cerebral ischaemic patients

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Background and Purpose: Blood oxygenation level dependent contrast functional magnetic resonance imaging (BOLD-fMRI) has been applied to functional mapping in brain disorders, based on the assumption that normal adults and patients with brain disorders exhibit similar evoked cerebral blood oxygenation (CBO) changes. This study compared evoked CBO changes measured by near infrared spectroscopy (NIRS) with the activation mapping obtained by BOLD-fMRI in patients with cerebral ischaemia.

Methods: The study involved six normal adults and six patients with cerebral ischaemia. Hand grasping was performed as a motor task. All patients could perform the task similarly to the controls at the time of examination, but single photon emission computed tomography demonstrated low baseline cerebral blood flow and a decreased haemodynamic reserve in the primary sensorimotor cortex on the lesion side. Using NIRS, concentration changes of deoxyhaemoglobin (Deoxy-Hb), oxyhaemoglobin (Oxy-Hb), and total haemoglobin (Total-Hb) were measured in the primary sensorimotor cortex contralateral to the task. BOLD-fMRI signals were measured by 1.5 T magnetic resonance imaging using an echo-planar technique. Activation maps were calculated by statistical parametric mapping.

Results: In the controls, Deoxy-Hb decreased in association with increases of Oxy-Hb and Total-Hb in the primary sensorimotor cortex during the task. However, in the patients, Deoxy-Hb increased significantly from baseline, while Oxy-Hb and Total-Hb also increased, indicating the presence of rCBF increases in response to neuronal activation. BOLD-fMRI demonstrated only limited activation areas in the primary sensorimotor cortex on the lesion side.

Conclusion: The CBO changes in patients with cerebral ischaemia differed from those of normal adults; Deoxy-Hb was increased in activation areas of the patients. This implies that BOLD-fMRI may overlook activation areas in the patients unless both increases and decreases of signal are taken into consideration.

Blood oxygenation level dependent contrast functional MRI (BOLD-fMRI) images areas of activation by detecting a reduced concentration of deoxyhaemoglobin (Deoxy-Hb),¹ which is caused by a larger increase in regional cerebral blood flow (rCBF) compared with the cerebral metabolic rate for oxygen in normal adults.² Based on the assumption that normal adults and patients with brain disorders exhibit similar evoked cerebral blood oxygenation (CBO) changes, BOLD-fMRI has been applied to the functional imaging of brain disorders.³ However, neuronal activation studies using near infrared spectroscopy (NIRS) have demonstrated that the evoked CBO changes in brain disorders differ from those of normal adults; in many stroke patients with aphasia, language tasks caused an increase of Deoxy-Hb, asso-

ciated with increases of oxyhaemoglobin (Oxy-Hb) and total haemoglobin (Total-Hb), in the left prefrontal cortex.⁴ In addition, recent BOLD-fMRI investigations on patients with brain tumours have cast doubt on the reliability of its functional imaging in such patients.⁵

In this study, using NIRS, we evaluated the CBO changes in the primary sensorimotor cortex (PSMC) of normal adults and cerebral ischaemic patients during motor tasks. In addition, we compared the evoked CBO changes and activation mapping obtained by BOLD-fMRI.

PATIENTS AND METHODS

Subjects

We studied six normal adults (28–68 years) and six patients with cerebral ischaemia (42–68 years). In the cerebral ischaemic patients, three cases had internal carotid artery occlusion, two had middle cerebral artery occlusion, and one had middle cerebral artery stenosis. Computed tomography (CT) or MRI was undertaken in each patient to obtain morphological information before the examination; one case showed cerebral infarction, whereas five cases showed no lesion. The clinical profiles of the patients are shown in table 1. Informed consent to participate in the study was obtained from each subject.

Methods

Hand grasping was performed as a motor task, and all patients could perform the task similarly to the controls at the time of examination (3 to 12 months after onset). We used a NIRO-300 monitor (Hamamatsu Photonics KK, Japan) to measure the concentration changes of Deoxy-Hb, Oxy-Hb, and Total-Hb in the PSMC contralateral to the task performance. The probes were placed at a distance of 3 cm or 4 cm on the head over the PSMC, so that the axis of the probes could be aimed to superimpose on the central sulcus; the point 2 cm posterior to the midposition of the arc extending from nasion toinion, to the point 5 cm straight up from the external auditory meatus.⁶ After carrying out the initial setting by this method, the position of the probes was adjusted so that the maximum responses of Oxy-Hb and Total-Hb were obtained during the task performance. In five normal subjects, the location of the probes was identified by MRI using vitamin E capsules.

BOLD-fMRI signals were measured by 1.5 T MRI (Symphony, Siemens, Germany) using an echo-planar technique; TE 50 ms, TR 4 s, slice thickness 3 mm, matrix size 40×40, FOV 192×192 mm. A total of 120 frames of 40 axial slices (acquisition time of one frame four seconds) through the PSMC were

Abbreviations: CBO, cerebral blood oxygenation; CBF, cerebral blood flow; NIRS, near infrared spectroscopy; BOLD-fMRI, blood oxygenation dependent contrast functional MRI; SPECT, single photon emission computed tomography; PSMC, primary sensorimotor cortex; Deoxy-Hb, deoxyhaemoglobin; Oxy-Hb, oxyhaemoglobin; Total-Hb, total haemoglobin

Table 1 Clinical profiles of the stroke patients

Patient	Age (y)/ sex	Clinical type of stroke	MRI/CT	Cause of stroke	Time from onset (months)
1	42/ M	TIA	Normal	Rt-MCA occlusion	5
2	68/ M	CS	CI (Rt-MCA territory)	Rt-C occlusion	12
3	60/ M	TIA	Normal	Lt-C occlusion	5
4	52/ F	TIA	Normal	Lt-MCA stenosis	3
5	68/ F	TIA	Normal	Lt-MCA occlusion	3
6	58/ M	TIA	Normal	Rt-C occlusion	3

TIA, transient ischaemic attack; CS, completed stroke; CI, cerebral infarction; IC, internal carotid artery; MCA, middle cerebral artery.

acquired during repeated motor task (40 seconds) and resting periods (40 seconds); this task-rest cycle was repeated six times. Activation maps were calculated by Statistical Parametric Mapping (SPM; Z score > 1.5).

To evaluate the baseline CBF and vascular reactivity in the patients, we performed single photon emission CT (SPECT; ECD-RVR method) at rest and at 10 minutes after intravenous injection of acetazolamide (1.0 g).

RESULTS

In the normal subjects, NIRS showed a decrease of Deoxy-Hb (-0.5 (0.2), mean (SD) in arbitrary units) associated with increases of Oxy-Hb (4.9 (1.2)) and Total-Hb (4.4 (0.9)) in the PSMC contralateral to the task performance (fig 1 (A) left). BOLD-fMRI showed robust activation areas in the PSMC contralateral to the performing hand (fig 1 (B) left).

In the cerebral ischaemic patients, NIRS showed an increase of Deoxy-Hb (1.2 (0.3)) in the PSMC on the lesion side during the contralateral motor task (fig 1 (A) right). Oxy-Hb (1.3 (0.6)) and Total-Hb (2.4 (0.7)) increased significantly from the baseline, indicating the presence of rCBF increases in response to neuronal activation. BOLD-fMRI showed only limited activation areas in the PSMC on the lesion side during the task (fig 1 (B) right).

SPECT showed a low baseline rCBF (27 (4.1) ml/g/min) in the PSMC on the lesion side of the patients. In addition, the

rCBF (28 (4.5) ml/g/min) in the PSMC on the lesion side did not increase significantly after acetazolamide injection.

DISCUSSION

One of the important findings obtained in this study was that, in patients with cerebral ischaemia, the focal concentration of Deoxy-Hb increased in the PSMC on the lesion side during the task, associated with increases of Oxy-Hb and Total-Hb, whereas Deoxy-Hb decreased in the controls. The increases in Oxy-Hb and Total-Hb suggest that the rCBF in the PSMC of the patients was increased during the motor task; this is consistent with the evoked rCBF response in ischaemic stroke observed by PET.⁷ The increase of Deoxy-Hb was evident during the entire course of the task, so that it differs from the Deoxy-Hb increase occurring within a few seconds after the start of neuronal activation,⁸ or the "post-stimulus overshoot" of Deoxy-Hb occurring in the visual cortex.⁹

In the cerebral ischaemic patients, BOLD-fMRI showed only limited area of activation in the PSMC on the lesion side. In addition to the task performance, the significant increases of Oxy-Hb and Total-Hb indicated an activation of the PSMC in the patients. These observations suggest that the BOLD-fMRI did not image the activation area correctly. Such a failure might be caused by the SPM, because it images the activation areas by detecting increases of BOLD signals (that is, decreases of Deoxy-Hb) during activation. Recently, a similar failure of

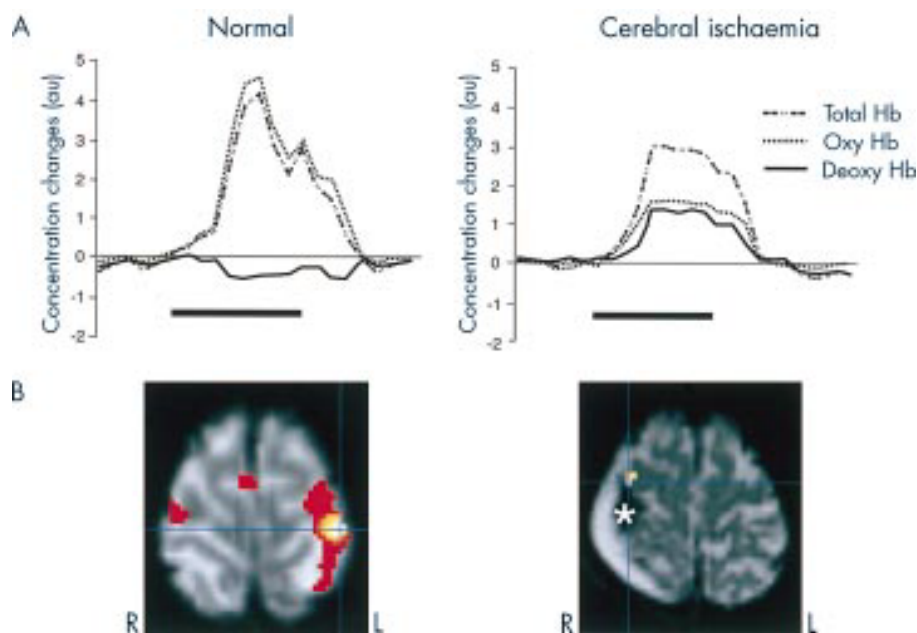


Figure 1 (A) CBO changes in the PSMC of the control and the cerebral ischaemic patient (68 years, right internal carotid artery occlusion, 12 months after onset) during contralateral motor tasks measured by NIRS. Deoxy-Hb decreased in the control, but increased in the patient. The ordinates indicate concentration changes of Oxy-Hb, Deoxy-Hb, and Total-Hb in arbitrary units (au). Horizontal thick bars indicate the period of the task. (B) Threshold activated areas superimposed onto T₂ images of the normal (right motor task) and the patient (left motor task). The asterisk in the right panel indicates a lesion of infarction.

functional imaging by BOLD-fMRI has been noted in patients with brain tumour.⁵ Although the evoked CBO changes were not evaluated in these brain tumour studies, in our preliminary investigations on brain tumours, we have found an increase of Deoxy-Hb in the PSMC adjacent to the brain tumour (unpublished data).

The underlying physiological mechanism of the Deoxy-Hb increase in the cerebral ischaemic patients remains unclear. In the stroke patients with aphasia, similar increases of Deoxy-Hb have been observed in the left prefrontal cortex during language tasks.⁴ We hypothesise that the cerebral oxygen consumption of the cerebral ischaemic patients may have been increased more by neuronal activity than in the normal adults. The oxygen consumption could increase in the activation area, if the activation area utilised the energy metabolism that requires oxygen, such as oxidation of lactate. SPECT showed a low baseline rCBF and a reduced cerebrovascular reactivity in the PSMC on the lesion side. These findings imply that metabolic acidosis occurred at rest, associated with the presence of lactate in the PSMC of the patients. Under such conditions, when oxygen was supplied through an increase of rCBF in response to neuronal activation, the lactate might have been oxidised, resulting in an increase of Deoxy-Hb. Indeed, in vitro studies have showed that lactate can serve as an aerobic energy substrate for neuronal activation induced by glutamate.¹⁰

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Competing interests: none declared.

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