Changes in Cerebral Blood Oxygenation Induced by Deep Brain Stimulation: Study by Near-Infrared Spectroscopy (NIRS)

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Abstract. Previous studies have demonstrated that neural activation causes changes in cerebral blood oxygenation (CBO), i.e. increases in tissue levels of oxy-Hb and total-Hb with a decrease in deoxy-Hb concentration. It is unclear, however, whether neural activation always induces the same pattern of CBO changes or not. In the present study, employing a near-infrared spectroscopy (NIRS), we investigated the CBO changes in the frontal lobe induced by direct stimulation of the thalamus (Vim) or globus pallidus (GPi) in patients with Parkinson’s disease or essential tremor. The results indicated that under conditions of neural activation in the frontal lobe, oxy-Hb and total-Hb increased in all 6 cases. Deoxy-Hb decreased in 2 cases during GPi stimulation, and increased in 4 cases during low frequency stimulation of the Vim. The above findings suggest that neural activation induces various patterns of CBO change, especially in deoxy-Hb. This implies that functional MRI based on the BOLD contrast may not consistently detect the area of neural activation.

Key words: cerebral blood oxygenation, near-infrared spectroscopy, functional MRI, deep brain stimulation

Introduction

Neural activation induces increases in regional cerebral blood flow (rCBF) and metabolism. Since the increase in rCBF exceeds the increase in tissue oxygen demands of activated brain tissue, the blood concentration of deoxy-Hb decreases while those of oxy-Hb and total-Hb increase. Functional MRI (fMRI) can detect such a deoxy-Hb decrease and provide images of the area of neural activation.

For the treatment of involuntary movements or bradykinesia in Parkinson’s disease or other diseases, we have employed deep brain stimulation therapy using a stimulation electrode implanted in the basal ganglia. Such cases provide a unique opportunity to investigate the changes in cerebral blood oxygenation (CBO) that accompany neural activation. In the present study, we examined the CBO changes in the frontal lobe induced by direct stimulation of the thalamus or globus pallidus utilizing near-infrared spectroscopy (NIRS).

Methods

We studied 6 patients; including 4 with Parkinson’s disease (PD) and 2 with essential tremor (ET), who underwent implantation of electrodes into the thalamus or globus pallidus. The electrodes were implanted at the thalamic nucleus ventralis intermedius (Vim) for the treatment of tremor, in 2 cases of PD and 2 cases of ET, or at the globus pallidus internus (GPi) for the treatment of bradykinesia in 2 cases of PD. The CBO changes were monitored in the bilateral frontal lobes employing NIRS (NIRO-300, Hamamatsu Photonics K.K.). The NIRO-300 provides continuous monitoring of the levels of oxy-Hb, deoxy-Hb and total (oxy- + deoxy-) Hb, reflecting changes in the regional CBO and CBF in the area beneath the probe.

Results

In GPi stimulation, the stimulus frequency was fixed at 120 Hz, and the stimulus intensity was increased from 0 V to 10 V in 1 V steps every 1 min. Stimulation at less than 5 V caused no remarkable changes in CBO. At over 6 V, the stimulation induced increases in oxy-Hb and total-Hb with a decrease in deoxy-Hb level (Figure 1). After termination of the electrical stimulation, these parameters quickly returned to their baseline levels. One of the 2 cases revealed larger CBO changes in the frontal lobe ipsilateral
to the stimulus side, while the other case showed similar levels of increase on both sides.

In Vim stimulation, the stimulus intensity was fixed at 3 V, and the stimulus frequencies were decreased from 100 Hz to 0 Hz in 10 Hz steps. The decrease in stimulus frequency induced oxy-Hb and total-Hb increases as well as a deoxy-Hb increase concomitant with the re-appearance of tremor (Figure 2). After restartnig the Vim stimulation at 100 Hz, and 3 V, CBO gradually returned to near-baseline levels.

Discussion

Previous PET studies have demonstrated that neural activation causes a 50% increase in rCBF, while the tissue oxygen consumption increases by only 5%. This imbalance between the cerebral circulation and metabolism results in an increase in blood concentration of oxy-Hb and a decrease in deoxy-Hb concentration in the activated brain. Functional MRI can detect such deoxy-Hb changes associated with neural activity (based on Blood Oxygenation Level Dependent (BOLD) contrast).

In the present cases of PD with bradykinesia, GPi stimulation induced an increase in oxy-Hb and a decrease in deoxy-Hb in the frontal lobe (Figure 1). This suggests that the frontal neurons were activated by direct stimulation of the GPi. In contrast, in the tremor cases, Vim stimulation decreased the oxy-Hb, total-Hb, as well as deoxy-Hb concentration (Figure 2), suggesting that frontal neuron activities were suppressed by direct stimulation of the Vim. Opposite deoxy-Hb responses of the frontal neurons could result from different actions of the neural connections between the GPi and frontal lobe, and between the Vim and frontal lobe. When the stimulus frequencies of the Vim were gradually decreased, oxy-Hb, deoxy-Hb and total-Hb were increased accompanied by the reappearance of tremor, suggesting that frontal neurons are activated in the presence of tremor. Such increases in deoxy-Hb in tremor cases could result from a large increase in tissue oxygen consumption which exceeds the rCBF increase.

In summary, under conditions of neural activation in the frontal lobe, oxy-Hb and total-Hb were increased in all 6 cases. Deoxy-Hb was decreased in 2 cases and increased in 4 cases. The present findings suggest that neural activation can induce various patterns of CBO change, especially in deoxy-Hb. This implies that fMRI based on the BOLD contrast may not consistently detect the area of neural activation.

References


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Cerebral Blood Flow on Xenon CT: Correlation with the Blood Flow Detected at the Common Carotid Artery on Ultrasonography

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Abstract. To correlate cerebral blood flow (CBF) on xenon CT with the flow at common carotid artery (CCA) detected by color doppler ultrasonography, 82 patients (29 men, 53 women; 20-90 yrs) were examined. They included normal volunteers (n=33), patients with cerebral infarction (n=8), multiple lacunar infarcts (n=12), dementia (n=14), and parkinson disease (n=15). Flow at the CCA was graded as extremely low (<0.3 l/min), low (0.3-0.4), and normal (>0.4). CBF was measured in the following distribution: anterior, middle, posterior cerebral arteries (ACA, MCA, PCA); white matter border zones (BZ); basal ganglia (BA), thalamus in two slices. CBF may be reduced in the BZ, cortical and deep gray matter with extremely low flow at CCA. We suggest that color doppler ultrasonography may aid in triage of patients for further CBF evaluation. As some overlap in CBF exists between normal and diseased groups with respect to low flow at CCA, color doppler ultrasonography must be evaluated in combination with xenon CT to reflect cerebral blood flow.

Key words: xenon CT, ultrasonography, cerebral blood flow, common carotid artery

Introduction

Xenon CT measurements of regional cerebral hemodynamics can predict risk for stroke.1-2 Large trials have been performed to correlate this risk with the ipsilateral carotid artery stenosis.3-5 However, as the hemodynamic effect of occlusive carotid disease on arterial flow to brain tissue depends upon not only the the degree of stenosis but also the adequacy of collateral circulatory pathways, the degree of carotid stenosis alone correlates poorly with the hemodynamic status of the ipsilateral cerebral circulation.6 7 In contrast, correlation between the flow at the common carotid artery (CCA) and cerebral blood flow (CBF) is potentially meaningful as the flow at CCA contains both the flow to brain and the collateral flow. Ultrasonography is of a diagnostic choice in the evaluation of patients with carotid artery disease.8 In this study we measure CBF in variable cerebral arterial distribution by xenon-CT, and correlate them with flow values at CCA obtained by color doppler ultrasonography.

Subjects and Methods

From July 1995 to November 1998, 82 patients (29 men, 53 women, aged 20-90 yrs with a mean of 71) were examined by both color doppler US and Xenon CT. They included normal volunteers (n=33), patients with cerebral infarction (n=8), multiple lacunar infarcts (n=12), dementia (n=14) and parkinson disease (n=15).

Toshiba X speed CT system incorporated with Az-723-BA (Anzai Medical) was used to analyze CBF data in two brain slices (namely, cranial slice and caudal slice) in parallel with orbitomeatal line. Caudal slice contains the structures of basal ganglia and thalamus, whereas the cranial slice transverses through the lateral ventricle. Examinations were made during inhalation of a gas mixture (33% stable xenon plus 67% oxygen) in a 4 min wash-in/6 min washout protocol. CBF was measured according to the following anatomic distribution: anterior cerebral artery (ACA), middle cerebral artery (MCA), posterior cerebral artery (PCA), white matter border zones (BZ) between ACA and MCA, and between MCA and PCA, basal ganglia (BA), thalamus in a symmetric pattern (Figure 1).

Blood flow at the CCA was measured by ultrasonography before Xenon CT examinations. Informed consent was obtained in all patients. CBF was then correlated with the flow at CCA detected by color doppler US by means of analysis of variances. Significance was tested by student t test. A P value of 0.05 was considered to indicate significance.
Results

1. Comparisons between two corresponding topographic CBF in variable ipsilateral CCA flow in normal volunteers and variable diseases do not reveal any significance (t test, p>0.05).

2. Comparisons of CBF and CCA flow in normal volunteers and variable diseases show CBF values in the BZ, ACA, MCA, PCA, basal ganglia, thalamus are significantly reduced when the flow at the ipsilateral right CCA is extremely low (<0.3 l/min) (p<0.0001). And some overlap exists between normal and variable diseases (Figure 2-4).

Conclusion

CBF may be reduced in the border zone, cortical and deep gray matter with extremely low flow at common carotid artery detected by color doppler ultrasonography in normal and variable diseases. We suggest that color doppler ultrasonography may aid in triage of patients for further CBF evaluation. As some overlap in CBF exists between normal and diseased groups with respect to low flow at common carotid artery, ultrasonography must be evaluated in combination with xenon CT to reflect cerebral blood flow.

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Figure 1 Caudal Slice
Cranial slice

Figure 2  Relationship between BZ CBF and right ipsilateral CCA flow

Figure 3  Relationship between MCA and right ipsilateral CCA flow
Figure 4  Relationship between BG CBF and right ipsilateral CCA flow