Cerebral Oxygenation in the Frontal Lobe Cortex during Incremental Exercise Tests: The Regional Changes Influenced by Volitional Exhaustion

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Abstract The present study examined the regional differences of cortical oxygenation in the frontal lobe by near-infrared spectroscopy (NIRS) during incremental exercise tests and the precise location of NIRS was examined by brain magnetic resonance imaging (MRI). Pulmonary gas exchange and NIRS measurement during incremental cycling ergometry tests were investigated in 14 men. In 7 of these subjects, the right middle cerebral artery mean velocity (MCA Vmean) was simultaneously measured by transcranial Doppler (TCD). In the right medial of the frontal lobe cortex, Tissue Oxygenation Index (TOI) increased by 8.8% with its peak value at respiratory compensation threshold (RCT) and Normalized Tissue Hemoglobin Index (nTHI) increased until end-point by 16.2%. During incremental exercise tests, the changing pattern of TOI was different according to the distribution of the probes. Volitional exhaustion by exercise induced the deteriorated TOI and MCA Vmean, whereas nTHI increased.

1 Introduction

Cerebral perfusion is affected by the mental effort to exercise which seems to be indicated by RPE (ratings of perceived exertion: Borg's scales) [1]. During exercise the mental effort is associated with the increase in cerebral oxygenation [2, 3]. Near-infrared spectroscopy can monitor tissue or capillary oxygenation of the brain non-invasively in real-time and thus has advantage for monitoring of the strenuous whole body exercise [4, 5]. Considering that the mental effort to exercise would enhance the cerebral activity which affects the regional cerebral blood flow (rCBF) or metabolic substrate such as glucose [6], the rCBF of the

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responsible areas for the mental effort to exercise would change in response to the work intensity or duration. Accordingly the cerebral oxygenation would be influenced by volitional exhaustion.

In the present study, we arranged the probes of NIRS in the forehead in tow ways. Purpose of this study was to (1) investigate dynamics of cerebral oxygenation and blood flow with respect to exercise intensity that was indicated by changes of cardiopulmonary variables during incremental exercise tests, (2) examine the regional differences for cortical oxygenation in the frontal lobe during exercise especially at volitional exhaustion.

2 Methods

Fourteen healthy male volunteers (Age = 20.5 ± 0.9 yr, height = 172.9 ± 3.5 cm, weight = 63.3 ± 7.4 kg) were recruited. The study was consistent with the Helsinki declaration and approved by the ethical committee of Tokyo Medical and Dental University. Subjects were divided in two groups by the distributions of the NIRS probes which were localized in 1) the right medial and the left medial regions (*group A*) and 2) the right medial and the right lateral regions (*group B*). Two groups were matched by age, height and weight. The probes were placed on the scalp over the right frontal lobe or the left frontal lobe (Fig. 1). Each subject performed an incremental exercise test on a cycle ergometer (Power Max, Combi) to volitional exhaustion. The subjects work rate was increased by 20 W every 1 min beginning from 20 W in *group A* (ramp

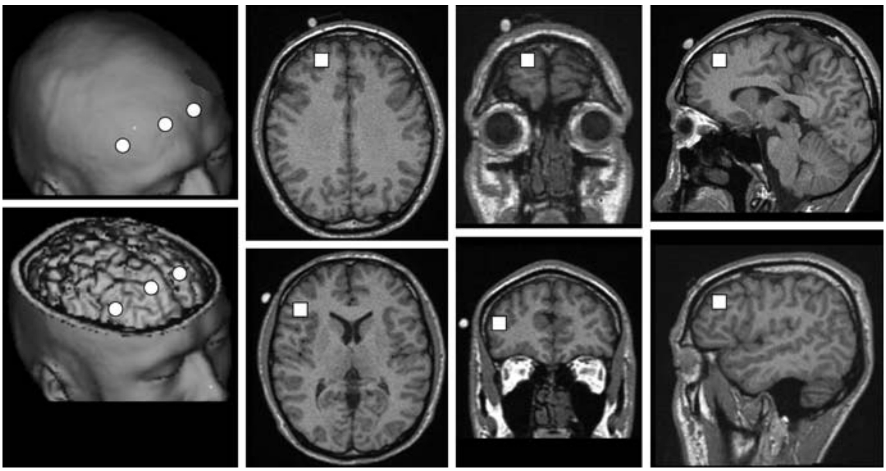

Fig. 1 Estimation of the localized portions of NIRS by MRI. *White circle*; the *center* of probe. *White square*; the estimated region in the *right* frontal lobe detected by NIRS. High intensity on the scalp showed the Vitamine E capsules as the marker of the probes

protocol) and by 30 W every 2 min beginning with 30 W in *group B* (stepwise protocol). RPE was recorded at every 2 min.

Metabolic CO_2 production (VCO_2), O_2 uptake (VO_2), and end-tidal CO_2 partial pressure ($P_{ET}CO_2$) were determined using cardiopulmonary exercise test systems (CPET, Cosmed or Mi-300, Minato). For each test, anaerobic threshold (AT) was determined by the V-slope method and respiratory compensation threshold (RCT) was determined based on the pulmonary gas exchange variables ($P_{ET}CO_2$, VE/VCO_2, and $\%FECO_2$) [7].

During exercise, cerebral blood oxygenation in the frontal lobe cortex was determined by NIRS (NIRO 200, Hamamatsu photonics). Variables of Tissue Oxygenation Index (TOI) and normalized Tissue Hemoglobin Index (nTHI) that are based on the spatially-resolved spectroscopy (SRS) method were used. Since the absolute value of TOI is dependent on the underlying tissue [8], relative change from the baseline (rest) (%) was induced. In seven subjects (*group B*), the right middle cerebral artery mean velocity (MCA Vmean) was measured simultaneously by transcranial Doppler (TCD) (Companion III, Nicolet Vascular).

In one subject, magnet resonance imaging (MRI) of the brain was obtained for the precise localization of NIRS probe positions with respect to the cortex anatomy (MAGNETOM Avanto, SIEMENS). In addition to 2D imaging, 3D reconstruction of scalp and brain surface was performed using the auto-mated software for fusion imaging (Dr.View, AJS).

The pulmonary gas exchange and NIRS measurements were time aligned and averaged over a 20 s interval for subsequent analysis. The MCA Vmean measurements were averaged over a 5 s interval at every one minute. Data are presented as mean $\pm$ SD and Pearson's correlation analysis was used to evaluate associations between variables. One-way repeated-measures ANOVA followed by Bonferroni post hoc evaluation for multiple comparisons were used to identify differences across exercise intensity. Relative changes in the NIRS variables over exercise intensity were compared between the regions by two-way repeated measures ANOVA. A P-value of 0.05 was considered statistically significant.

3 Results

The variables of at rest and at exercise intensity of 2 min, AT, RCT and endpoint are described in Table 1. In *group B* VO_2 and REP were higher at endpoint. RPE was different between the groups at 2 min due to the work rate inequality. VCO_2/VO_2 increased after RCT similarly between the groups. Between AT and RCT, VO_2 and VCO_2/VO_2 were differed but the others were similar. In the right medial frontal lobe cortex, TOI increased by $8.8 \pm 5.3\%$ from rest to maximum as nTHI ranged from 0.96 ± 0.09 to 1.15 ± 0.14. MCA Vmean ranged from 59.6 ± 16.2 cm/s to 79.8 ± 20.1 cm/s. $P_{ET}CO_2$ in *group A*

Table 1 Physiological responses, NIRS variables and MCAV mean at 2 min, anaerobic threshold, respiration threshold and endpoint

		Rest	2 min	AT	RCT	Endpoint
Exercise time (min) §	group A	–	120	266 ± 81	500 ± 135	581 ± 118
	group B	–	120	282 ± 35	508 ± 65	734 ± 121††
Work rate (W)	group A	–	60	109 ± 27	187 ± 45	213 ± 39
	group B	–	30	81 ± 15	154 ± 20	201 ± 33
VO_2 (ml / min / kg) §	group A	9.7 ± 0.9	13.4 ± 1.2	20.0 ± 2.6	31.0 ± 5.1‡‡‡	36.2 ± 3.8
	group B	8.1 ± 1.9	13.8 ± 1.5	23.1 ± 3.6†	33.6 ± 4.2‡‡	42.4 ± 6.5†††
VCO_2 / VO_2	group A	0.85 ± 0.05	0.85 ± 0.06	0.88 ± 0.06	1.01 ± 0.04 ***,‡‡	1.10 ± 0.08 ***
	group B	0.79 ± 0.07	0.79 ± 0.07	0.88 ± 0.04	1.03 ± 0.04 ***,‡‡	1.13 ± 0.07 ***
$P_{ET}CO_2$ (mmHg)	group A	42.4 ± 1.5	44.2 ± 2.8	48.6 ± 2.7 **	50.1 ± 2.4 ***	47.7 ± 3.6 **
	group B	38.3 ± 3.3	42.1 ± 3.1	46.4 ± 5.0 *	46.1 ± 5.4 *	42.7 ± 6.2
RPE§§§	group A	6	9.6 ± 1.0	12.1 ± 0.9	14.9 ± 2.0	16.9 ± 0.9
	group B	6	6.9 ± 0.7††	10.6 ± 2.4	14.9 ± 1.9	18.8 ± 0.8†
ΔTOI (%)	Rt medial [a, b]	0	2.2 ± 3.0	4.2 ± 3.8	8.8 ± 5.3 ***	6.8 ± 5.9 ***
	Lt medial [a]	0	1.3 ± 1.1	2.9 ± 2.2	5.5 ± 2.8 ***	4.3 ± 3.0
	Rt lateral [b]	0	–0.8 ± 2.2	–0.5 ± 2.2	1.4 ± 5.3	4.0 ± 8.4
nTHI	Rt medial [a, b]	0.99 ± 0.08	1.01 ± 0.09	1.04 ± 0.10	1.11 ± 0.11 *	1.15 ± 0.14 **
	Lt medial [a]	0.97 ± 0.09	0.96 ± 0.10	0.98 ± 0.11	1.06 ± 0.13	1.12 ± 0.10
	Rt lateral [b]	1.02 ± 0.04	1.02 ± 0.04	1.00 ± 0.04	1.03 ± 0.05	1.13 ± 0.16
MCA Vmean (cm /sec)		59.6 ± 16.2	68.4 ± 18.4 *	78.7 ± 21.1 ***	79.8 ± 20.1 ***	71.3 ± 18.6 **

Values are mean ± SD derived from group A ($n = 7$) and B ($n = 7$).
[a] From group A ($n = 7$), [b] group B and [a, b] the both group combined ($n = 14$).
AT = anaerobic threshold; RCT = respiratory compensation threshold; $P_{ET}CO_2$ = end-tidal CO_2 partial pressure; RPE = ratings of perceived exertion (Borg's scale : 6–20); ΔTOI = Relative changes from resting conditions of Tissue Oxygenation Index (%); nTHI = normalized Tissue hemoglobin Index (relative value); MCA Vmean = mean velocity of the right middle cerebral artery.
*, **, and *** Significantly different versus rest, $P < 0.05$, 0.01 and 0.001, respectively.
‡‡ and ‡‡‡ Significantly different versus AT, $P < 0.01$ and 0.001, respectively.
§ and §§§ Significant interaction (group * exercise), $P < 0.05$ and 0.001, respectively.
† ,†† and ††† Significantly different from group A at this point, $P < 0.05$, 0.01 and 0.001, respectively.

ranged from 42.4 ± 1.5 mmHg to 50.1 ± 2.4 mmHg and $P_{ET}CO_2$ in *group B* from 38.3 ± 3.3 mmHg to 46.4 ± 5.0 mmHg. In 6 of 7 subjects, the relative change of MCA Vmean correlated with $P_{ET}CO_2$ (r^2 = 0.47 to 0.85). In 11 of 14 subjects, TOI and nTHI of the right medial correlated with $P_{ET}CO_2$ (r^2 = 0.09 to 0.81 and r^2 = 0.13 to 0.67, respectively). In the lateral region, TOI and nTHI did not correlated well with $P_{ET}CO_2$. As shown in Fig. 1, the medial and the lateral region of the NIRS probe correspond to the superior frontal gyrus (SFG) and the inferior frontal gyrus (IFG), respectively.

The relative changes from the baseline (rest) (%) of NIRS variables are shown in Fig. 2. In the regions of right medial and lateral frontal lobe (*group B*), there was a significant interaction (region ∗ intensity) for TOI with difference at endpoint. TOI of the right medial increased significantly at RCT with tendency of the decline at endpoint, whereas nTHI, except for the right lateral, increased significantly at RCT and endpoint with their peaks at endpoint.

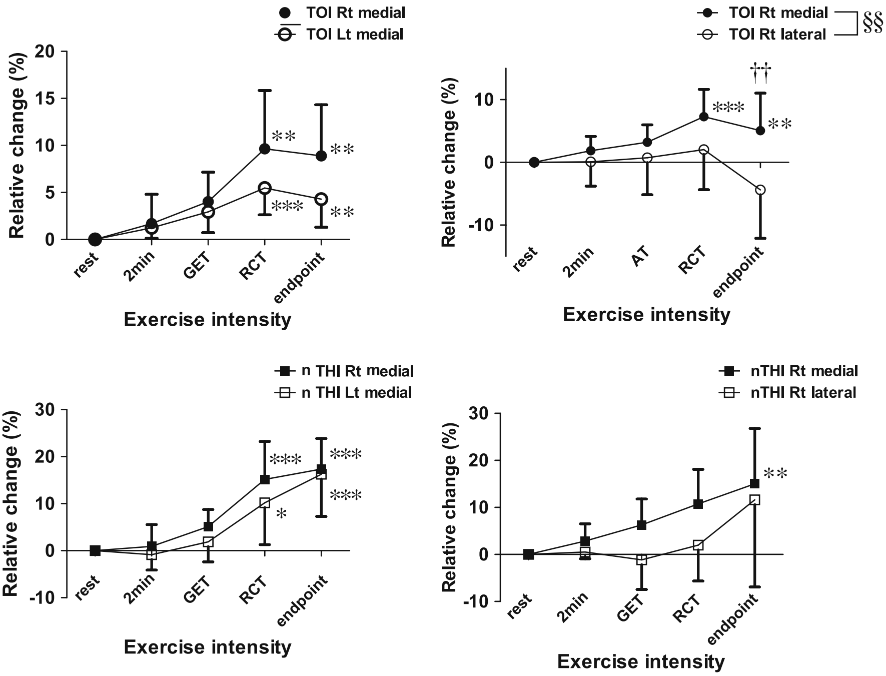

Fig. 2 Changes in NIRS variables at rest, 2 min, AT, RCT and endpoint for the region of the *right* medial (Rt medial) and the *left* medial (Lt medial) of the frontal lobe (group A, *left* side) and the *right* medial (Rt medial) and lateral (Rt lateral) (group B, *right* side). Values are mean ± SD. **, and ***Significantly higher than rest values, $P < 0.05$, 0.01 and 0.0001, respectively. §§Significantly different from TOI Rt medial at this point, $P < 0.01$

4 Discussion

We described the dynamic change of the cerebral oxygenation in the frontal lobe during exercise. VO_2 and RPE differed at endpoint, suggesting that exercise capacity of subjects was higher in *group B*. Despite the difference of the exercise protocols, exercise intensity based on gas exchange [7] was similar between two groups and this was reflected in the similar VCO_2/VO_2. Between AT and RCT, variables from brain were similar with VO_2 and VCO_2/VO_2 differed. The changing pattern of the two groups TOI in the right medial was similar ($F = 0.003$, $P = 0.42$). Cerebral oxygenation derived from NIRS has relationship with rCBF [9, 10], however neither TOI nor nTHI reflected rCBF directly. Since the arterial saturation, artery to venous ratio and oxygen consumption are required to obtain rCBF from TOI [11], rCBF could be speculated by changes of other factors. When exercise intensity exceeded RCT, a finding that TOI and nTHI in the right SFG increased implies increases of rCBF if nTHI had derived from arterial fraction. If not, with rCBF stable, we could speculate that decreases of oxygen consumption affected increases of TOI. When exercise intensity below RCT, a small increase in $P_{ET}CO_2$ would support the increase in CBF and MCA Vmean [12]. Our data were concomitant with this association of $P_{ET}CO_2$ and MCAV mean, whereas $P_{ET}CO_2$ correlated to some extent with TOI and nTHI in the SFG and did not well in the IFG. Considering the possible association of TOI and nTHI with rCBF, it implies that $P_{ET}CO_2$ would affect rCBF differently among the MCA perfusion areas and the frontal lobe regions.

Major finding of this study is the regional difference between the SFG and the IFG. Matching MRI with NIRS makes it possible to relate results to regional gyral anatomy on an individual basis [13]. With regard to the mental effort to exercise, activation of anterior cingulate cortex was demonstrated [14, 15]. Considering that the SFG in the present study was close to the region of interest defined as the anterior cingulated cortex in the previous studies, the SFG would be activated due to the mental effort exercise. The difference in the oxygenation between the SFG and the IFG at volitional exhaustion suggested that the SFG was activated related to sense of effort or central command and the IFG was not activated.

In conclusion, we described that the cerebral oxygenation changed with exercise intensity during incremental exercise tests and that the changing patterns of the cerebral oxygenation between two gyri in the frontal lobe were different.

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