Forearm Oxygen Consumption and Forearm Blood Flow in Healthy Children and Adolescents Measured by Near Infrared Spectroscopy

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Abstract: The assessment of forearm oxygen consumption ($\dot{V}O_2$) and forearm blood flow (FBF) by means of near infrared spectroscopy has become widespread in adults, whereas in children and adolescents no data are available. The aim of the present study was to analyze $\dot{V}O_2$ and FBF in healthy children and adolescents. Methods: In a prospective cohort study, 20 male and 20 female healthy children and adolescents were investigated. The measurements of $\dot{V}O_2$ and FBF were performed by means of near infrared spectroscopy in combination with the venous occlusion method. Results: Mean $\dot{V}O_2$ was 0.08 ± 0.04

ml $100\text{ g}^{-1}\text{ min}^{-1}$ in male and 0.09 ± 0.05 ml $100\text{ g}^{-1}\text{ min}^{-1}$ in female subjects. Mean FBF was 1.95 ± 1.25 ml $100\text{ g}^{-1}\text{ min}^{-1}$ in male and 1.82 ± 0.98 ml $100\text{ g}^{-1}\text{ min}^{-1}$ in female subjects. No significant difference was found between male and female subjects. A significant negative correlation of $\dot{V}O_2$ and FBF to age was observed in both groups. Conclusion: In the present study we were able to show that $\dot{V}O_2$ and FBF decreased with increasing age in children and adolescents without significant differences between male and female subjects.

Key words: near infrared spectroscopy, forearm oxygen consumption, forearm blood flow, development.

Near infrared spectroscopy (NIRS) is a relatively new method, which is noninvasive and continuous and operates in real time, thus enabling in-vivo monitoring of tissue oxygenation and hemodynamics. NIRS has been applied to measure the oxygenation and hemodynamics of a variety of tissues, including muscle, brain, and connective tissue. With an adequate optode separation (more than 20 mm), the skin and the subcutaneous fat constitutes less than 5% of the signal measured over a given body segment in lean subjects [1, 2]. The NIRS signal therefore predominately reflects the microcirculation and O_2 availability of tissue, which is dependent on interoptode distance, 2–6 cm deep [1]. Thus by positioning the optodes on the forearm, NIRS enables the measurement of the oxygenation and hemodynamics of forearm muscle.

The venous occlusion, another noninvasive method, in combination with NIRS has been validated and has become an accepted method for the assessment of forearm muscular oxygen consumption ($\dot{V}O_2$) [3–5] and forearm blood flow (FBF) [6]. Nevertheless, most studies on muscle oxygenation and hemodynamics were performed on healthy adults and adult patients [1, 4, 7] and on term and preterm neonates [8, 9]. In a recent study we analyzed FBF in children and adolescents with type I diabetes and healthy children and adolescents [6].

The aim of the present study was the measurement and analysis of $\dot{V}O_2$ and FBF of forearm muscle in healthy children and adolescents.

METHODS

Children and adolescents aged from 6 to 18 years were studied. The subjects, who were obese, i.e., body mass index (BMI) beyond the 90th percentile, or who had taken any medicaments within the past seven days, were excluded. Male and female subjects were matched for age (± 6 months). Each subject was a volunteer, and informed consent was obtained from all parents and adolescents before we started measurements. The study was approved by the local ethical committee.

NIRS measurements were carried out with the NIRO 300 (Hamamatsu Photonics, Japan). This equipment includes four laser diodes for measurements with wavelengths of 775, 825, 850, and 904 nm. The optodes were placed over the brachioradial muscle of the left forearm 4 cm distal of the elbow, the interoptode distance was 3.5 cm, and the sampling rate was 2/s. A differential path length factor of 4.16 was used [10]. NIRS enables the non-invasive continuous measurement of changes in the concentration of oxygenated hemoglobin ($\Delta cHbO_2$), deoxygenated hemoglobin (ΔcHb), and cytochrome oxidase ($\Delta cCytO_x$). NIRS parameters were measured in μM units.

$\dot{V}O_2$ was calculated by evaluating the rate of the increase of ΔcHb converted into ml $O_2/100\text{ g/min}$. Mean forearm density was estimated at 1.04 kg l^{-1} [11].

FBF was calculated from the linear increase of cHb_{tot} during venous occlusion measured by NIRS, taking into account the hemoglobin value of each subject. Further-

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more, the molecular weight (64.458 g/mol) and the molecular ratio between hemoglobin and oxygen (1:4) were taken into account. FBF was expressed in ml/100 g muscle/min.

For venous occlusion a pneumatic cuff was placed around the arm above the elbow. The subjects were sitting in a comfortable chair. The left arm was placed at the level of the right atrium. Heart rate and peripheral arterial oxygen saturation were measured by pulse oximetry, whereby the sensor was placed on the third finger of the left hand.

After the placements of the optodes, pneumatic cuff, and oximetry, there was a 10-min rest period. The measurement of blood pressure was then performed. After a rest period of 1 min, again the pneumatic cuff was inflated within 0.5–1 s to a pressure, which was below the diastolic arterial pressure and above the venous pressure. The cuff was maintained inflated for 20 s. This procedure was repeated three times with a rest period of 40 s between the inflations. To define $\dot{V}O_2$ and FBF in each subject, we calculated the mean of the three measurements. Hemoglobin concentrations of blood were analyzed from a blood sample.

For a comparison of male and female subjects, the data of $\dot{V}O_2$ and FBF at rest were compared by the unpaired Student's *t*-test. For comparison of the three measurements of $\dot{V}O_2$ and FBF at rest, the paired Student's *t*-test was used, respectively. $\dot{V}O_2$ and FBF were correlated to age, arm circumference, standard deviation score of BMI [12], hemoglobin concentration, heart rate, oxygen saturation, and arterial blood pressure by linear and polynomial regression analysis. The data are represented as mean $\pm$ SD, if not stated otherwise. The level of statistical significance was set at $p < 0.05$. All statistical analyses of recorded data were performed with Statview 4.5 Software.

Fig. 1. Oxygen consumption ($\dot{V}O_2$) at rest in 20 healthy male children and adolescents. Significant correlation of age to $\dot{V}O_2$. $Y = 0.185 - 0.008 * X$; $r = 0.66$, $p = 0.001$.

RESULTS

A total number of 40 children and adolescents, 20 male and 20 female subjects, were measured (Table 1). $\dot{V}O_2$ and FBF were similar in male and female subjects. Furthermore, no significant differences could be observed in any of the analyzed parameters between the subjects (Table 1).

The three consecutive measurements of $\dot{V}O_2$ (0.08 ± 0.05 ; 0.09 ± 0.04 ; 0.09 ± 0.05 ml 100 g muscle⁻¹ min⁻¹; n.s.) and FBF (1.86 ± 1.05 ; 1.91 ± 1.14 ; 1.90 ± 0.95 ml 100 g muscle⁻¹ min⁻¹; n.s.) within subjects showed high reproducibility.

$\dot{V}O_2$ was significantly correlated to age, whereby $\dot{V}O_2$ decreased with increasing age (Figs. 1 and 2). FBF also decreased with increasing age (Figs. 3 and 4). $\dot{V}O_2$ and FBF did not correlate to any of the other analyzed variables, i.e., arm circumference, standard deviation score of BMI, hemoglobin concentration, heart rate, oxygen saturation, and arterial blood pressure (n.s.).

Table 1. Twenty healthy male and 20 healthy female children and adolescents.

	Mean $\pm$ SD		
	Male, <i>n</i> = 20	Female, <i>n</i> = 20	
$\dot{V}O_2$, ml 100 g ⁻¹ min ⁻¹	0.08 $\pm$ 0.04	0.09 $\pm$ 0.05	n.s.
FBF, ml 100 g ⁻¹ min ⁻¹	1.95 $\pm$ 1.25	1.82 $\pm$ 0.98	n.s.
Age, years	12.5 $\pm$ 2.9	12.8 $\pm$ 3.1	n.s.
Body weight, kg	45.1 $\pm$ 14.7	46.2 $\pm$ 12.6	n.s.
Height, cm	152.5 $\pm$ 16.5	154.3 $\pm$ 16.5	n.s.
Body mass index (BMI)	18.8 $\pm$ 2.9	19.1 $\pm$ 2.8	n.s.
Standard deviation score (BMI)	0.01 $\pm$ 0.85	-0.01 $\pm$ 1.07	n.s.
Arm circumference, cm	23.2 $\pm$ 3.7	23.1 $\pm$ 2.8	n.s.
Hemoglobin concentration, g/dl	13.3 $\pm$ 1.7	13.3 $\pm$ 1.4	n.s.
Heart rate/min	87 $\pm$ 12	87 $\pm$ 14	n.s.
Oxygen saturation, %	98 $\pm$ 0.5	98 $\pm$ 0.2	n.s.
Systolic blood pressure, mmHg	99 $\pm$ 12	97 $\pm$ 9	n.s.
Diastolic blood pressure, mmHg	58 $\pm$ 10	56 $\pm$ 7	n.s.

Forearm Oxygen Consumption

Fig. 2. Oxygen consumption (VO_2) at rest in 20 healthy female children and adolescents. Significant correlation of age to VO_2 . $Y = 0.184 - 0.008 * X$; $r = 0.45$, $p = 0.048$.

Fig. 4. Forearm blood flow (FBF) at rest in 20 healthy female children and adolescents. Significant correlation of age to FBF. $Y = 3.93 - 0.16 * X$; $r = 0.51$, $p = 0.026$.

Fig. 3. Forearm blood flow (FBF) at rest in 20 healthy male children and adolescents. Significant correlation of age to FBF. $Y = 5.24 - 0.27 * X$; $r = 0.80$, $p < 0.001$.

With increasing age, the arm circumference also increased ($r = 0.52$, $p = 0.0006$). The other parameters were independent of age (n.s.). No change of SaO_2 or heart rate was observed during venous occlusion.

DISCUSSION

The present study was the first that showed the age dependency of VO_2 in healthy children and adolescents with no difference between male and female subjects. VO_2 decreased with increasing age. FBF decreased with increasing age, too, as we have recently reported [6].

In regard to the positioning and penetration depth of NIRS, which is about half of the interoptode distance [1, 11], the measurements of a particular tissue region, namely, the brachioradial muscle, were performed in all subjects. VO_2 and FBF of this particular region were independent of arm circumference, which is a measure of the whole size of the arm.

Recent studies demonstrated that adipose tissue thickness (from 1 to 10 mm) correlates with FBF and VO_2 , whereby VO_2 decreases and FBF increases with increasing adipose tissue thickness [11]. In the present study, adi-

pose tissue thickness was not measured; therefore a possible influence on results cannot be clearly ruled out. Nevertheless, we found a decrease of FBF with increasing age that suggests a negligible influence of the increasing adipose tissue thickness with increasing age on the changes of FBF and VO_2 . The increase of the adipose tissue thickness in European children aged from 6 to 10 years was described to be about 0.5 to 1.5 mm [13]. Furthermore, since obese subjects were excluded in the present study, the influence of the overlying skin and the subcutaneous fat can be assumed to be less than 5% [1, 2]. This is supported by the missing correlation of VO_2 and FBF to BMI and the standard deviation score of BMI.

In the present study, no influence of heart rate, blood pressure, or oxygen saturation has been observed. According to literature, muscular perfusion and as a consequence oxygen supply are mainly influenced by local vasoactive compounds, i.e., acetylcholine, NO, and adenosine [14].

The comparison of the present values of VO_2 and FBF to studies in adults is difficult. VO_2 in adult varies from 0.05 to 0.23 ml 100 g muscle⁻¹ min⁻¹ [15]. The variety of FBF is similar [1, 4, 5]. The reason for this variety might be the factors used in calculation. First the differential path length factor varies from 2.6 to 4.57 [2, 4]. Second, the factor for muscle density varies from 1.04 kg l⁻¹ [4, 15] to 1.14 kg l⁻¹ [16]. Furthermore, we find a different positioning of optodes in comparing the studies. Since NIRS measures local VO_2 and FBF, which may be different in different muscle groups, the place where the optodes are positioned have an effect on the obtained values [5]. In the present study, the same factors were used in all subjects, and the optodes were positioned in the same way that makes the obtained data comparable.

In adults a great variability between subjects and high reproducibility within them have been reported [4]. Similar observations could be made in the present study with high reproducibility within subjects. The variability between subjects, however, was mainly age related, which

may be due to the ongoing development of the muscle during childhood.

Little is known about the development of the skeletal muscle system during childhood and adolescence. Causes of the observed present age-dependent changes might be changes in muscle cross-sectional area and metabolism during growth that is still discussed as being controversial [17–21]. A comparison of muscular fatigue of boys and of adult men suggests that more fatigable Type 2 fibers are involved in men, resulting in greater lactic acid and ion accumulation during fatigue [18]. Children rely less on glycolysis than adults do during high-intensity exercise, leading to a lower production of lactate during intense cycling [19].

With the present data, the reason for the age dependency of $\dot{V}O_2$ and FBF cannot be ruled out, but the findings of the age dependency of $\dot{V}O_2$ and FBF are important. In further studies the present observations of $\dot{V}O_2$ and FBF in children and adolescents must be taken into account.

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