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Relationship of middle cerebral artery blood flow velocity to intensity during dynamic exercise in normal subjects

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Summary. Cerebral blood flow has been reported to increase during dynamic exercise, but whether this occurs in proportion to the intensity remains unsettled. We measured middle cerebral artery blood flow velocity (v_m) by transcranial Doppler ultrasound in 14 healthy young adults, at rest and during dynamic exercise performed on a cycle ergometer at a intensity progressively increasing, by 50 W every 4 min until exhaustion. Arterial blood pressure, heart rate, end-tidal, partial pressure of carbon dioxide ($P_{ET}CO_2$), oxygen uptake ($\dot{V}O_2$) and carbon dioxide output were determined at exercise intensity. Mean v_M increased from 53 (SEM 2) $cm \cdot s^{-1}$ at rest to a maximum of 75 (SEM 4) $cm \cdot s^{-1}$ at 57% of the maximal attained $\dot{V}O_2$ ($\dot{V}O_{2max}$), and thereafter progressively decreased to 59 (SEM 4) $cm \cdot s^{-1}$ at $\dot{V}O_{2max}$. The respiratory exchange ratio (R) was 0.97 (SEM 0.01) at 57% of $\dot{V}O_{2max}$ and 1.10 (SEM 0.01) at $\dot{V}O_{2max}$. The $P_{ET}CO_2$ increased from 5.9 (SEM 0.2) kPa at rest to 7.4 (SEM 0.2) kPa at 57% of $\dot{V}O_{2max}$, and thereafter decreased to 5.9 (SEM 0.2) kPa at $\dot{V}O_{2max}$. Mean arterial pressure increased from 98 (SEM 1) mmHg (13.1 kPa) at rest to 116 (SEM 1) mmHg (15.5 kPa) at 90% of $\dot{V}O_{2max}$, and decreased slightly to 108 (SEM 1) mmHg (14.4 kPa) at $\dot{V}O_{2max}$. In all the subjects, the maximal value of v_m was recorded at the highest attained exercise intensity below the anaerobic threshold (defined by R greater than 1). We concluded that cerebral blood flow as evaluated by middle cerebral artery flow velocity increased during dynamic exercise as a function of exercise intensity below the anaerobic threshold. At higher intensities, cerebral blood flow decreased, without however a complete return to baseline values, and it is suggested that this may have been at least in part explained by concomitant changes in arterial PCO_2.

Key words: Transcranial Doppler ultrasound – End-tidal carbon dioxide tension – Dynamic exercise – Oxygen uptake – Anaerobic threshold

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Introduction

As recently reviewed by Jorgensen et al. (1992), most studies using methods designed to reflect cortical flow have reported an increase in cerebral blood flow ($\dot{Q}_{cer}$) during dynamic exercise and no change in $\dot{Q}_{cer}$ during static exercise. It has been shown that movement-associated increases in $\dot{Q}_{cer}$ are blunted by local anaesthesia of the exercising limb (Friedman et al. 1991), and that muscle ischaemia does not affect $\dot{Q}_{cer}$ (Jorgensen et al. 1992). These observations would suggest that $\dot{Q}_{cer}$ during dynamic exercise depends mainly on the activation of mechanoreceptors (Jorgensen et al. 1992). If so, $\dot{Q}_{cer}$ during dynamic exercise should not be greatly affected by the intensity. However, limited and discrepant data are available on the relationship between $\dot{Q}_{cer}$ and intensity during dynamic exercise (Herholz et al. 1987; Thomas et al. 1989; Jorgensen et al. 1992).

The purpose of the present study was to evaluate the effects of exercise intensity on $\dot{Q}_{cer}$ during dynamic exercise in normal subjects. The $\dot{Q}_{cer}$ was estimated by transcranial Doppler ultrasound (TCD) determinations of middle cerebral artery flow velocity (v_m). Recent studies have shown an excellent agreement between TCD and the ^{133}Xe clearance method of measuring changes in $\dot{Q}_{cer}$ during dynamic exercise (Jorgensen et al. 1992). The advantages of TCD over the reference ^{133}Xe clearance method are its noninvasive character and its ability to detect repeatedly rapid changes in $\dot{Q}_{cer}$.

Methods

Subjects. A group of 14 healthy young male subjects aged 20–25 years (mean 24 years) gave informed consent to the study which was approved by the Ethics Committee of the Erasme University Hospital. Their body masses ranged from 58 to 90 kg (mean 70 kg) and their heights from 163 to 185 cm (mean 173 cm). Physical examination, chest X-ray and electrocardiogram were all normal. None of them were cigarette smokers and none of them had taken any medication for at least 1 week prior to the study.

Protocol. Dynamic exercise was performed with the subjects seated on an electrically braked cycle ergometer (Siemens Ergometry System 380 C). The pedalling frequency was kept between 50 and 70 rpm throughout each exercise test. The intensity was increased by 50 W every 4 min until exhaustion. Ventilation ($\dot{V}_E$), respiratory rate (f_R), oxygen uptake ($\dot{V}O_2$), carbon dioxide output ($\dot{V}CO_2$), respiratory exchange ratio (R), end-tidal partial pressure of carbon dioxide ($P_{ET}CO_2$), mean systematic arterial presure ($\overline{BP}_a$), heart rate (f_c) and v_m were measured at baseline (0 W) and at the end of every 4-min period at each successive exercise intensity.

Measurements. The subjects breathed through a face mask connected to a heated pneumotachograph of the Lilly type, for the measurements of $\dot{V}_E$ and f_R. The expired air was collected in a plastic bag for the measurement of mixed expired concentrations of O_2 (by a zirconium cell) and CO_2 (by an infrared cell) (Ergopneumotest Jäeger, E. Jäeger Co., Hoechberg, Germany). A correction for instrument dead space (40 ml) and temperature were made in the computation of $\dot{V}O_2$ and $\dot{V}CO_2$ which were displayed together with $\dot{V}_E$, f_R, intensity and R every 15 s on a screen. Measurements during 1 min at the baseline and during the last minute at each exercise intensity were averaged. The P_{ET}-CO_2 was measured using a Datex CNO-103 Multicap (Instrumentarium Corp., Helsinki, Finland). Blood pressure was measured by a sphygmomanometer and f_c was determined from an electrocardiogram lead which was monitored continuously.

The v_m of TCD was measured using a 2-Mhz pulsed Doppler (Trans-Scan, EME, Überlingen, Germany). Skin, hair and probe were coated with gel. The probe was secured with a headband at the posterior temporal window. The proximal segment of the middle cerebral artery was insonated at a depth of 50–55 mm and maintained throughout the exercise test. Mean middle cerebral flow velocity (v_m) was determined as the mean velocity of time-averaged maximal velocity over the cardiac cycle computed from the envelope of the maximal frequencies of the Doppler spectra in 3-s periods by the equipment. A pulsatility index (PI) was calculated as the difference between systolic and diastolic velocity divided by v_m (Aaslid 1986). The v_m of TCD was followed continuously and recorded during 30 s at rest and during the last 30 s of each exercise intensity.

Statistics. Statistical analysis consisted of a repeated measures analysis of variance. When the F-ratio reached a $P<0.05$ critical value, modified student's t-tests were performed to compare different intensities of exercise (Winer 1971).

Results

The highest exercise intensity which was achieved was 200 W for 2 subjects, 250 W for 5 subjects and 300 W for 7 subjects. Values for the variables at different intensities of exercise expressed as a percentage of the maximal attained $\dot{V}O_2$ ($\dot{V}O_{2max}$) are shown in Table 1. The change in of v_m and $P_{ET}CO_2$ in relation to $\dot{V}O_2$ is illustrated in Fig. 1.

The v_m increased in proportion to exercise intensity up to about 60% of $\dot{V}O_{2max}$ ($P<0.01$), and thereafter decreased ($P<0.01$), without however returning to the baseline value ($P<0.05$, $\dot{V}O_{2max}$ vs baseline). In contrast, PI increased progressively up to $\dot{V}O_{2max}$ ($P<0.01$). The $\dot{V}_E$, $\dot{V}O_2$, $\dot{V}CO_2$, R and f_c increased along with the increase in exercise intensity ($P<0.01$). It may be noted that R was greater than 1 at an exercise intensity corresponding to more than 60% of

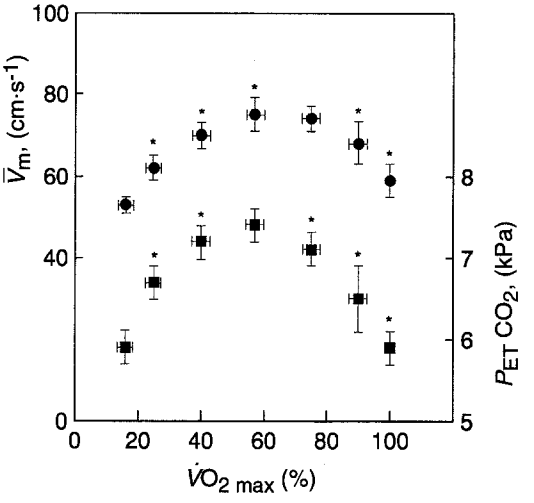

Fig. 1. Mean and SEM values for mean middle cerebral artery flow velocity ($\bar{v}_m$) (*circles*) and end-tidal partial pressure of carbon dioxide ($P_{ET}CO_2$) (*squares*) in 14 normal subjects during dynamic exercise of progressively intensity up to maximal oxygen uptake ($\dot{V}O_{2max}$). * $P<0.05$ compared to the preceding exercise intensity

Table 1. Values for mean velocity of the middle cerebral artery ($\bar{v}_m$), pulsatility index (PI), minute ventilation ($\dot{V}_E$), carbon dioxide output ($\dot{V}CO_2$), oxygen uptake ($\dot{V}O_2$), respiratory exchange ratio (R), end tidal partial pressure of carbon dioxide ($P_{ET}CO_2$), mean systemic arterial pressure ($\overline{BP}_a$) and heart rate (f_c)

$\dot{V}O_2$, % of $\dot{V}O_{2max}$	mean 16 ($n=14$)	SEM 1	mean 25 ($n=14$)	SEM 1	mean 40 ($n=13$)	SEM 2	mean 57 ($n=14$)	SEM 2	mean 75 ($n=11$)	SEM 2	mean 90 ($n=8$)	SEM 2	mean 100 ($n=14$)	SEM 0
v_m (cm·s^{-1})	53	2	62	3	70	3	75	4	74	3	68	5	59	4
PI	1.2	0.1	1.4	0.1	1.5	0.1	1.6	0.1	1.6	0.1	1.8	0.1	2.0	0.1
$\dot{V}_E$ (l·min^{-1})	16	1	21	1	33	1	46	1	65	2	92	4	112	4
$\dot{V}CO_2$ (ml·min^{-1})	517	23	714	23	1273	24	1872	45	2611	65	3470	102	3752	118
$\dot{V}O_2$ (ml·min^{-1})	617	13	831	24	1371	18	1922	44	2586	44	3269	85	3402	117
R	0.84	0.01	0.86	0.01	0.93	0.01	0.97	0.01	1.01	0.01	1.06	0.01	1.10	0.01
$P_{ET}CO_2$ (kPa)	5.9	0.2	6.7	0.2	7.2	0.2	7.4	0.2	7.1	0.2	6.5	0.4	5.9	0.2
$\overline{BP}_a$ (mmHg)	98	1	104	1	110	1	112	1	114	1	116	1	108	1
(kPa)	13.1	0.13	13.9	0.13	14.7	0.13	14.9	0.13	15.2	0.13	15.5	0.13	14.4	0.13
f_c (beats·min^{-1})	76	3	95	3	120	3	146	4	167	3	181	3	187	3

$\dot{V}O_{2max}$. The $P_{ET}CO_2$ increased up to 60% of $\dot{V}O_{2max}$ ($P<0.01$), and thereafter decreased ($P<0.01$). The $P_{ET}CO_2$ at $\dot{V}O_{2max}$ was not different from baseline $P_{ET}CO_2$ (NS). The $\overline{BP}_a$ increased up to 90% of $\dot{V}O_{2max}$ ($P<0.01$) and thereafter slightly decreased ($P<0.05$). Systolic arterial pressure increased progressively from 115 (SEM 2) mmHg (15.3 kPa) at baseline to 174 (SEM 1) mmHg (23.2 kpA) at 90% of $\dot{V}O_{2max}$ ($P<0.01$), to decrease slightly to 162 (SEM 1) mmHg (21.6 kPa) at $\dot{V}O_{2max}$ ($P<0.05$). Diastolic arterial pressure remained unchanged from 85 (SEM 1) mmHg (11.3 kPa) at baseline to 86 (SEM 1) mmHg (11.5 kPa) at 90% of $\dot{V}O_{2max}$ (NS), with a slight decrease to 81 (SEM 1) mmHg (10.8 kPa) at $\dot{V}O_{2max}$.

There was no correlation between $\overline{BP}_a$ and v_m ($r=0.07$, NS). A moderately good correlation was found between $P_{ET}CO_2$ and v_m ($r=0.33$, $P<0.01$) and between PI and arterial pulse pressure ($r=0.31$, $P<0.01$).

Discussion

The present study showed that during dynamic exercise of progressive intensity in normal subjects, $\dot{Q}_{cer}$ (evaluated by v_m) increased in proportion to the intensity as long as it remained below the anaerobic threshold, and thereafter tended to return to the resting baseline level.

As recently reviewed by Jorgensen et al. (1992) and by Thomas et al. (1989), dynamic exercise has been reported either not to affect, to increase or to decrease $\dot{Q}_{cer}$ in studies based on the nitrous oxide method, which measures an average blood flow through the whole brain. It has only been after the advent of the ^{133}Xe-washout technique measuring cortical blod, that it has been demonstrated that dynamic exercise is associated with an increase in $\dot{Q}_{cer}$ (Thomas et al. 1989; Jorgensen et al. 1992). However, whether this occurs in proportion to exercise intensity remains unsettled. Cerebral hemisphere $\dot{Q}_{cer}$ has been shown to increase by 15% in patients with minor neurological deficits but normal arteriography when performing repeated and vigorous hand contractions (Olesen 1971). Comparable increases in $\dot{Q}_{cer}$ have been found in 16 normal subjects exercising both legs in a semirecumbant position on a cycle ergometer, suggesting that muscle mass plays little role in the changes in $\dot{Q}_{cer}$ during dynamic exercise (Thomas et al. 1989). In that same study, there was no relationship between the dynamic exercise-induced increase in $\dot{Q}_{cer}$ and exercise intensity from 32% to 86% of $\dot{V}O_{2max}$ (Thomas et al. 1989). This was confirmed by Jorgensen et al. (1992) who have reported an average increase in $\dot{Q}_{cer}$ of 25% in 10 normal subjects who exercised at two levels of dynamic exercise, corresponding to f_c around 110 beats·min^{-1} and 148 beats·min^{-1}. These findings however are at variance with those of Herholz et al. (1987) who have shown that $\dot{Q}_{cer}$ in 12 young men exercising on a cycle ergometer increased by 13.5% at 25 W and by 24.7% at 100 W. These discrepancies may be explained by the fact that the relationship between exercise intensity and $\dot{Q}_{cer}$ has not until now been investigated in detail at several intensities of exercise up to $\dot{V}O_{2max}$.

The advantages of the TCD measurement of v_m over the ^{133}Xe-washout method in evaluating exercise-induced changes in $\dot{Q}_{cer}$ are:

1. Total non-invasiveness, allowing a large number of measurements during a given exercise test
2. Ability to detect rapid changes in cerebral perfusion
3. Absence of the necessity to keep the head in a fixed position (Jorgensen 1992).

Methodological limitations in the number of measurements, and an increase of the level of error with head movement, would explain why previous studies using the ^{133}Xe-washout method have been limited to a maximum of two measurements of $\dot{Q}_{cer}$ at two intensities of submaximal dynamic exercise (Herholz et al. 1987; Thomas et al. 1989; Jorgensen et al. 1992). An inspection of the $\dot{V}_E$, expired gas and f_c measurements in these studies would indicate that no measurements of $\dot{Q}_{cer}$ above the anaerobic threshold were performed.

The $\dot{Q}_{cer}$ has been shown to increase in proportion to the metabolic demand of brain tissue (Raichle et al. 1976). Increased local cerebral metabolic demand during exercise could be the result of either generated neural activity or "central command" and/or nonspecific arousal stimuli from the contracting muscles or moving limbs (Jorgensen et al. 1992). It has been found that static exercise does not increase $\dot{Q}_{cer}$ (Rogers et al. 1990; Friedman et al. 1991; Jorgensen et al. 1992). Muscle ischaemia has been shown not to be accompanied by an increase in $\dot{Q}_{cer}$ (Jorgensen et al. 1992). A movement-associated increase in $\dot{Q}_{cer}$ was found to be attenuated or suppressed by regional anaesthesia of the exercising limb (Friedman et al. 1991). There are data which have suggested that a dynamic exercise-induced increase in $\dot{Q}_{cer}$ is not related to muscle mass or to exercise intensity (Thomas et al. 1989). Altogether, these studies would support the idea that a dynamic exercise-induced increase in $\dot{Q}_{cer}$ essentially depends on the activation of mechanoreceptors (Jorgensen et al. 1992). The present results would suggest that activation of other receptors within the working muscles may play a role in an intensity-related increase in $\dot{Q}_{cer}$ during dynamic exercise.

An increase in $\overline{BP}_a$ accounting for changes in $\dot{Q}_{cer}$ during dynamic exercise has been previously described by Herholz et al. (1987), but this would seem unlikely in this case, since $\overline{BP}_a$ has been shown to increase markedly during static exercise without any change in $\dot{Q}_{cer}$, and since muscle ischaemia which has increased $\overline{BP}_a$ more than exercise has not affected $\dot{Q}_{cer}$ either (Jorgensen et al. 1992). In addition, no correlation between $\overline{BP}_a$ and v_m was found in the present study. On the other hand, our subjects presented an increase in PI which was related to exercise intensity up to $\dot{V}O_{2max}$. This observation, also reported by Jorgensen et al. (1992), was probably explained by a concomitant increase in arterial pulse pressure.

A problem in the interpretation of the present results is that $P_{ET}CO_2$ did not remain constant. The $\dot{Q}_{cer}$ is well-known as being very sensitive to arterial PCO_2 (Shapiro et al. 1966) and is therefore usually corrected for arterial PCO_2 or $P_{ET}CO_2$. The $P_{ET}CO_2$ during dynamic exercise of progressive intensity has been shown to increase at moderate intensities of exercise above arterial PCO_2, and thereafter to remain parallel to it (Wasserman and Whipp 1975). The increase in $P_{ET}CO_2$ at moderate intensities of exercise is explained by an increase in the slope of the alveolar phase of expired CO_2 resulting from the increase in $\dot{V}CO_2$. Arterial PCO_2 normally remains constant up to the anaerobic threshold, and thereafter decreases because of lactic acidosis-induced augmentation of $\dot{V}_E$ (Wasserman and Whipp 1975). Therefore, in our subjects, in spite of an increase in $P_{ET}CO_2$, v_m was unlikely to have been affected by arterial PCO_2 below the anaerobic threshold. However, above the anaerobic threshold, at least part of the decrease in v_m was accounted for by arterial hypocapnia. We did not correct v_m for $P_{ET}CO_2$ using previously suggested equations (Markwalder et al. 1984), because $P_{ET}CO_2$ has been found not to provide a reliable determination of arterial PCO_2 at moderate intensities of exercise (Wasserman and Whipp 1975), and because such corrections are still less well-established for v_m of TCD than for ^{133}Xe-washout measurements (Jorgensen et al. 1992), and have not yet been validated in exercise.

The $\bar{v}_m$ changes have been shown to correspond to volume flow changes if vessel diameter is constant (Kontos 1989). Regional $\dot{Q}_{cer}$ increases during dynamic exercise have been found to correspond only to the motor-sensory cortex (Roland and Lassen 1976; Friedman et al. 1991). The middle cerebral artery has been demonstrated to serve about 80% of hemispheric flow including the motor-sensory cortex (Toole 1990). The excellent agreement between v_m and the initial slope of the ^{133}Xe-washout curve which has previously been reported during dynamic exercise (Jorgensen et al. 1992) would suggest that, at least up to the anaerobic threshould, dynamic exercise does not change middle cerebral artery diameter. Although it has been shown angiographically that the diameter of basal cerebral arteries remains constant during changes in inspired PCO_2 (Huber and Handa 1967), it cannot be ignored that higher intensities of exercise may affect the diameter of the middle cerebral artery, and thereby the validity of v_m of TCD to measure changes in $\dot{Q}_{cer}$.

In conclusion, the present study showed that $\dot{Q}_{cer}$ increased during dynamic exercise in proportion to exercise intensity below the anaerobic threshold. The observation that $\dot{Q}_{cer}$ decreased almost returning to resting levels at higher exercise intensities might be explained by concomitant changes in arterial PCO_2.

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