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Arm blood flow and metabolism during arm and combined arm and leg exercise in humans

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The cardiovascular response to exercise with several groups of skeletal muscle suggests that work with the arms may decrease leg blood flow. This study evaluated whether intense exercise with the legs would have a similar effect on arm blood flow ($\dot{Q}_{arm}$) and O_2 consumption ($\dot{V}_{O_2,arm}$). Ten healthy male subjects (age 21 ± 1 year; mean $\pm$ S.D.) performed arm cranking at 80 % of maximum arm work capacity (A trial) and combined arm cranking with cycling at 60 % of maximum leg work capacity (A + L trial). The combined trial was a maximum effort for 5–6 min. $\dot{Q}_{arm}$ measurement by thermodilution in the axilliary vein and arterial and venous blood samples permitted calculation of $\dot{V}_{O_2,arm}$. During the combined trial, $\dot{Q}_{arm}$ was reduced by 0.58 ± 0.25 l min^{-1} (19.1 ± 3.0 %, $P < 0.05$) from the value during arm cranking (3.00 ± 0.46 l min^{-1}). The arterio–venous O_2 difference increased from 122 ± 15 ml l^{-1} during the arm trial to 150 ± 21 ml l^{-1} ($P < 0.05$) during the combined trial. Thus, $\dot{V}_{O_2,arm}$ (0.45 ± 0.06 l min^{-1}) was reduced by 9.6 ± 6.3 % ($P < 0.05$) and arm vascular conductance from 27 ± 4 to 23 ± 3 ml min^{-1} (mmHg)$^{-1}$ ($P < 0.05$) as noradrenaline spillover from the arm increased from 7.5 ± 3.5 to 13.8 ± 4.2 nmol min^{-1} ($P < 0.05$). The data suggest that during maximal whole body exercise in humans, arm vasoconstriction is established to an extent that affects oxygen delivery to and utilisation by working skeletal muscles.

In humans, it is not established whether sympathetic vasoconstriction influences blood flow in active skeletal muscles. It has been argued that because of local regulation of muscle blood flow during exercise sympathetic control is lost (Remensnyder *et al.* 1962; Donald *et al.* 1970). However, evidence of such sympathetic vasoconstriction in active muscle has been reported (Saito *et al.* 1992; Kagaya, 1993; Kagaya *et al.* 1994). In these studies calf blood flow was reduced when fatiguing handgrip exercise was added to ongoing plantar flexion exercise.

Perfusion of the quadriceps muscles or the whole leg has been studied extensively during exercise. A dynamic exercise knee-extensor model or cycling has been used to evaluate the perfusion of the thigh, i.e. the quadriceps muscles, or of the whole leg. Blood flow values that have been measured in the leg are in the range of 6–9 l min^{-1}, which may represent a perfusion of 300–400 ml (100 g)$^{-1}$ min^{-1} (Andersen & Saltin, 1985; Rowell *et al.* 1986; Richardson *et al.* 1993). If these muscle perfusion values were to be attainable for the whole human musculature, a net cardiac output ($\dot{Q}$) of about 100 l min^{-1} (~3 times as high as the highest $\dot{Q}$ measured) would be required to maximally perfuse all skeletal muscle during maximal whole body exercise. Since blood pressure always increases with exercise intensity, even when involving the whole body musculature as occurs during combined arm and leg

exercise (Bevegård *et al.* 1966; Stenberg *et al.* 1967; Secher *et al.* 1977), it could be assumed that a certain degree of systemic vasoconstriction must take place. The intense sympathetic activity developed during heavy exercise results in differentiated vasoconstriction in, for example, the splanchnic circulation (Perko *et al.* 1998). However, it is not clear from the human data whether the increased sympathetic activity also affects working skeletal muscle perfusion. Secher *et al.* (1977) showed that when arm cranking is added to cycling (a combined exercise intensity of ~77 % of maximal oxygen uptake ($\dot{V}_{O_2,max}$), leg blood flow was reduced. However, subsequent studies that attempted to reproduce Secher's results did not show any evidence of neurogenic vasoconstriction during whole body exercise (Savard *et al.* 1989; Richter *et al.* 1992; Richardson *et al.* 1995; Bangsbo *et al.* 1997). Even though a reduction in leg vascular conductance was observed, there was no significant change in leg blood flow when arm exercise was added to leg exercise. Furthermore, an attempt to maximise sympathetic activation by static or ischaemic arm exercise affected leg vascular conductance, but not leg blood flow (Strange, 1999).

Data on arm blood flow ($\dot{Q}_{arm}$) and metabolism during arm exercise are limited. Ahlborg & Jensen-Urstad (1991*a*,*b*) measured $\dot{Q}_{arm}$ and metabolism at rest and during arm cranking up to 78 % of $\dot{V}_{O_2,max}$). They infused

cardiogreen into the brachial artery and measured its concentration in blood withdrawn from the axillary vein as an expression of $\dot{Q}_{arm}$. Blood flow increased linearly with workrate and $\dot{V}_{O_2}$ in most subjects, or it reached a plateau in some cases. Since the sympathetic activity, expressed as plasma levels of catecholamines during exercise, is proportional not only to the exercise intensity but also to the active muscle mass (Savard *et al.* 1989), it would be expected that the addition of leg to arm exercise would induce a greater increase in sympathetic activity than the addition of arm to leg exercise. Indeed, Secher *et al.* (1977) showed that the addition of cycling to arm cranking increased the oxygen extraction of the arm when working at the same work rate. Since an increased oxygen extraction is a response mechanism, aiming to maintain tissue oxygen uptake when delivery is limited, it also suggests a blood flow reduction was taking place. However, Secher *et al.* (1977) did not measure $\dot{Q}_{arm}$. The aim of the present study was to evaluate whether $\dot{Q}_{arm}$ and $\dot{V}_{O_2,arm}$ decrease when leg exercise is added to arm exercise at a given work rate.

METHODS

Following informed written consent ten healthy males (age 21 ± 1 year, height 183 ± 4 cm, weight 82 ± 3 kg, mean $\pm$ S.D.) participated in the study. The study was approved by the Copenhagen Ethics Committee (KF 01-314/97) and performed according to the Declaration of Helsinki. The subjects were physically active but not arm trained. All subjects were in the post-prandial phase when they reported to the laboratory and had been asked to refrain from any caffeine-containing products and intense physical activity on the previous day.

Experimental protocol

Following arterial and venous catheterisation of the non-dominant arm, the subjects performed in random order an A trial and an A + L trial for 5–6 min each. The maximum ~5 min work capacities and $\dot{V}_{O_2,max}$ for the two exercise modes as well as for cycling had been determined in previous laboratory visits (A, 153 ± 10 W; cycling, 345 ± 20 W). Arm cranking was performed on a modified friction-braked cycle ergometer (Monark, Stockholm, Sweden), while cycling was performed on an electrically braked ergometer (Elema, Stockholm, Sweden). The arm cranking frequency was metronome paced at 70 revolutions min^{-1}. The subjects were seated upright on the cycle ergometer with the arm cranking ergometer placed in front of them at a height and distance that ensured full arm extension in the horizontal position. Before the two trials, the subjects warmed up for 15 min using A + L at 40 % of the combined arm and leg work capacity. During the A trial the work intensity was 80 % of the arm work capacity. During the A + L trial, the work intensity for arm cranking was kept the same as in the A trial, while cycling at ~60 % of work capacity was added. All subjects reached their limits of exercise tolerance in 5–6 min during the A + L trial that required ~95 % of the subject's $\dot{V}_{O_2,max}$. A recovery period of 15 min was used between the two trials. The subjects were asked to use their arms equally during cranking so that the blood flow measurement would be representative of both arms.

A bolus thermodilution technique was used to measure $\dot{Q}_{arm}$. Under local anaesthesia, a pulmonary artery catheter (Swan-Ganz

132F5, Baxter Healthcare Corporation, Irvine, CA, USA) was introduced into the vena basilica at the elbow and advanced so that the thermistor was lying in the axillary vein. It was important to verify that the catheter was advanced enough to register flow from both the basilic and cephalic veins, but not advanced into the caval vein. To confirm this placement the following procedure was performed. A 5 ml bolus of saline at room temperature was injected into another catheter introduced into the cephalic vein of both arms. When saline was injected into the same arm as the Swan-Ganz catheter the blood temperature changed, while a similar injection into the catheter of the other arm had no effect. Three millilitres of room temperature saline boluses were infused and the temperature change was monitored with an Explorer Cardiopulmonary Hemodynamic Monitor (Baxter Healthcare) to ensure a monophasic thermodilution curve with an exponential decay. The bolus method provides similar values of $\dot{Q}_{arm}$ to those obtained by constant infusion of cooled saline (correlation coefficient, $r = 0.89$, $P < 0.01$, P. Krustrup, unpublished data).

During the first 3 min of each trial, measurements of $\dot{Q}_{arm}$ were taken every 15 s. After the first 3 min of each trial, samples (3–10 ml) of arterial and venous blood were drawn anaerobically over 10–20 s, from the tip of the catheter and from a catheter placed in the radial artery of the same arm for blood-gas, metabolites, and plasma catecholamine analyses. Following blood sampling, additional flow measurements were taken until the completion of the trial. Thus, for each trial the arm blood flow was expressed as the average of 10–12 separate measurements. Even though there was no statistical difference between measurements taken before and after blood sampling, measurements from the first minute were excluded from the calculation to ensure that the initial phase of rapid blood flow elevation was not included in the averaging. Nevertheless, it should be emphasised that both exercise trials represent unsteady state conditions.

Blood variables

Haemoglobin, oxygen and carbon dioxide tensions (P_{O_2} and P_{CO_2}), oxygen saturation (S_{O_2}), lactate, glucose, potassium, sodium and calcium were determined on an ABL blood analyser (model 700 Radiometer, Copenhagen, Denmark). Duplicate analyses from the same blood sample were made and the mean value of the two determinations was reported. Plasma adrenaline and noradrenaline (NA) levels were determined by a high-pressure liquid chromatography method with electrochemical detection. The rate of spillover of NA into plasma was determined as previously reported using flow rates, haematocrit, the difference in NA concentration between axilliary venous and arterial plasma, and the fractional extraction of adrenaline (Esler *et al.* 1990).

Central cardiovascular variables

The pulse contour method (Modelflow) was used to estimate the beat-to-beat changes in $\dot{Q}$ from the intra-radial arterial pressure input. This method uses a haemodynamic, non-linear, three-element model that relates the arterial pressure or pressure difference to a flow or volume via the impedance through which the flow is driven. The resultant flow waveform is integrated per beat to yield stroke volume that is multiplied by the heart rate (HR) to estimate $\dot{Q}$ (Wesselling *et al.* 1983). The model can be expressed as:

$$\dot{Q} = HR \times A_{sys} \times 1/Z_{ao},$$

where A_{sys} is the area under the systolic portion of the pressure wave and Z_{ao} the characteristic impedance of the aorta estimated from the age, mean pressure and heart rate. During exercise $\dot{Q}$

Table 1. Arm metabolic responses to arm (A) and combined arm plus leg exercise (A+L)

	Rest	A	A + L
O_2 content, arterial (ml l^{-1})	200 ± 4	211 ± 5	214 ± 5
Venous (ml l^{-1})	128 ± 9	98 ± 5 *	73 ± 6 * †
(a–v) diff. (ml l^{-1})	59 ± 4	122 ± 15 *	150 ± 21 * †
pH, arterial	7.42 ± 0.01	7.35 ± 0.02 *	7.31 ± 0.02 * †
Venous	7.35 ± 0.02	7.21 ± 0.02 *	7.16 ± 0.02 * †
P_{CO_2}, arterial (kPa)	4.69 ± 0.00	4.00 ± 0.00 *	4.00 ± 0.10 *
Venous (kPa)	6.19 ± 0.10	7.59 ± 0.00 *	7.90 ± 0.05 *
HCO_3^-, arterial (mM)	22 ± 0	17 ± 1 *	15 ± 1 * †
Venous (mM)	27 ± 0	24 ± 0 *	22 ± 1 * †
Lac, arterial (mM)	0.8 ± 0.1	7.0 ± 0.9 *	11.3 ± 1.2 * †
Venous (mM)	1.1 ± 0.1	10.1 ± 1.2 *	12.8 ± 1.4 * †
(a–v) diff. (mM)	−0.1 ± 0.1	−3.2 ± 0.5 *	-1.7 ± 0.3 * †
Release (mmol min^{-1})	0.0 ± 0.0	7.4 ± 0.6 *	3.7 ± 0.6 * †
Glu, arterial (mM)	4.9 ± 0.3	4.7 ± 0.2	5.1 ± 0.2
Venous (mM)	5.2 ± 0.1	5.2 ± 0.2	5.4 ± 0.2
(a–v) diff. (mM)	−0.3 ± 0.2	−0.5 ± 0.2	-0.2 ± 0.2 †
Release (mmol min^{-1})	0.1 ± 0.1	1.6 ± 0.8	0.7 ± 0.4
K^+, arterial (mM)	3.7 ± 0.2	4.5 ± 0.3 *	5.4 ± 0.3 * †
Venous (mM)	4.5 ± 0.1	6.1 ± 0.2 *	7.0 ± 0.4 * †
(a–v) diff (mM)	−0.8 ± 0.1	−1.6 ± 0.3 *	-1.6 ± 0.3 *
Release (mmol min^{-1})	0.3 ± 0.0	4.5 ± 1.1 *	3.4 ± 0.7 *
Na^+, arterial (mM)	140 ± 0	144 ± 1 *	145 ± 1 *
Venous (mM)	140 ± 1	145 ± 0 *	146 ± 0 *
(a–v) diff (mM)	1 ± 0	−1 ± 0	0 ± 0
Release (mmol min^{-1})	0 ± 0	3 ± 1	1 ± 1
Ca^{2+}, arterial (mM)	1.14 ± 0.02	1.19 ± 0.03	1.25 ± 0.03 * †
Venous (mM)	1.29 ± 0.01	1.39 ± 0.02 *	1.39 ± 0.02 *
(a–v) diff (mM)	−0.14 ± 0.02	−0.19 ± 0.04	−0.14 ± 0.03
Release (mmol min^{-1})	0.02 ± 0.01	0.53 ± 0.16 *	0.31 ± 0.09 *

Values are means ± S.E.M.; ($n = 10$). (a–v) diff., arterial–axilliary venous oxygen difference; pH, H^+ concentration; P_{CO_2}, carbon dioxide partial pressure; HCO_3^-, bicarbonate; Lac, lactate; Glu, glucose; K^+, potassium; Na^+, sodium; Ca^{2+}, calcium. * Different from rest, $P < 0.05$; † different from A, $P < 0.05$.

values obtained by the Modelflow method are comparable to those obtained by dye dilution (Ide *et al.* 1998).

Pulmonary gas exchange was measured with an Oxyscreen (CPX/D; Medical Graphics Corporation, St. Paul, Minnesota) metabolic cart and 15 s averaged values are reported. The HR was measured with a Vantage NV pulse watch (Polar Electro OY, Kempele, Finland). Mean arterial pressure (MAP) was obtained from the arterial catheter connected to a pressure monitoring kit (Baxter Healthcare Corporation, Irvine, CA, USA) positioned at the level of the heart with continuous infusion of isotonic saline (3 ml h^{-1}). Arm vascular conductance was reported as the ratio between $\dot{Q}_{arm}$ and MAP. For the calculation of arm vascular conductance, it was assumed that the influence of muscle contractions on blood flow was the same at a given work load and revolution rate.

Data are presented as mean ± S.E.M. for the whole exercise period. One-way ANOVA with repeated measures and Bonferroni *post hoc* test was used to assess differences between rest and the two exercise trials. For the meta-analysis of earlier relevant studies the Glass's effect size was used to compare results across studies. For continuous quantitative outcomes the standardised mean difference divided by the standard deviation was used as an index of effect size, as described by Hedges & Olkin (1985). A summary of weighted effect sizes and 95 % confidence intervals (CI) for all the studies were calculated. Statistical significance was set at $P < 0.05$.

RESULTS

The arm workload was 122 ± 8 W during both trials while, during the A + L trial, the leg work load was 207 ± 12 W. The $\dot{V}_{O_2}$ increased from 0.31 ± 0.01 l min^{-1} at rest to 2.36 ± 0.89 l min^{-1} during the A trial and to 3.85 ± 0.18 l min^{-1} during the A + L trial (~95 % of $\dot{V}_{O_2,max}$ measured during combined exercise; 4.04 ± 0.28 l min^{-1}).

Carbon dioxide ($\dot{V}_{CO_2}$) and minute ventilation ($\dot{V}_E$) increased in a similar fashion from 0.24 ± 0.01 and 9 ± 3 l min^{-1}, respectively, at rest to 2.59 ± 0.14 and 77 ± 6 l min^{-1}, respectively, during the A trial. During the A + L trial $\dot{V}_{CO_2}$ and $\dot{V}_E$ rose even higher to 4.12 ± 0.21 and 115 ± 3 l min^{-1} respectively. Similarly, HR increased from 77 ± 4 beats min^{-1} at rest to 147 ± 6 beats min^{-1} during the A trial and to 187 ± 3 beats min^{-1} during the A + L trial. The MAP increased from 83 ± 1 mmHg at rest to 112 ± 2 mmHg

during the A trial and fell to 103 ± 2 mmHg during the A + L trial. The $\dot{Q}$ was increased from 6.2 ± 0.3 l min^{-1} at rest to 14.1 ± 0.6 and 23.8 ± 0.7 l min^{-1} during the A and A + L trials, respectively.

At rest $\dot{Q}_{arm}$ was 0.35 ± 0.04 l min^{-1} and it increased to 3.00 ± 0.46 l min^{-1} during the A trial. During the A + L trial, $\dot{Q}_{arm}$ was 0.58 ± 0.25 l min^{-1} lower than during the A trial (19.1 ± 3.0 %). The arterio–venous oxygen difference increased from 59 ± 4 ml l^{-1} at rest to 122 ± 15 ml l^{-1} in the A trial and to 150 ± 21 ml l^{-1} during the A + L trial (Fig. 1). The arm vascular conductance was increased from 5 ± 0 ml min^{-1} (mmHg)$^{-1}$ at rest to 27 ± 4 ml min^{-1}

(mmHg)$^{-1}$ during the A trial and to 23 ± 3 ml min^{-1} (mmHg)$^{-1}$ during the A + L trial. Thus, $\dot{V}_{O_2,arm}$ was 0.45 ± 0.06 l min^{-1} during the A trial, but it was reduced by 9.6 ± 6.3 % to 0.40 ± 0.06 l min^{-1} during the A + L trial.

Arterial pH decreased from 7.42 ± 0.01 at rest to 7.35 ± 0.02 during the A trial and to 7.31 ± 0.02 during the A + L trial (Table 1). Similarly, pH of blood from the axillary vein decreased from 7.35 ± 0.02 at rest to 7.21 ± 0.02 and to 7.16 ± 0.02 during the A and A + L trials, respectively. During the A + L trial there was a steep increase in lactate concentration in arterial blood compared with the A trial. However, the increase of the
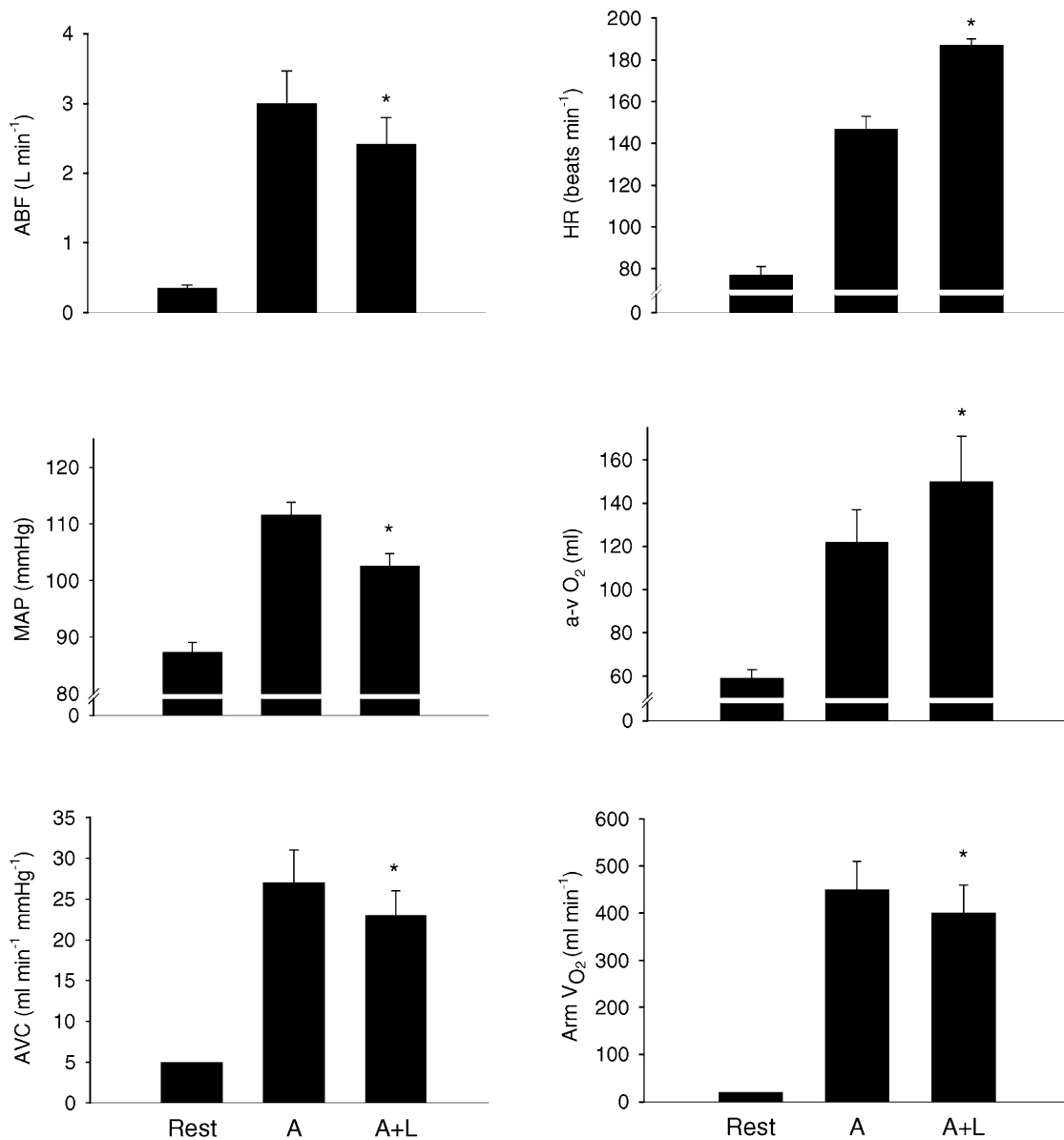

Figure 1. Central and regional cardiovascular and metabolic responses to arm (A) and combined arm and leg (A + L) exercise

ABF, arm blood flow; HR, heart rate; MAP, mean arterial pressure; a–v O$_2$, arterio–venous oxygen difference; AVC, arm vascular conductance, Arm $\dot{V}_{O_2}$, arm oxygen consumption. Values are means ± S.E.M.; $n = 10$. * Different from A, $P < 0.05$.

venous lactate concentration, even though significant, was moderate and lactate release from the arm decreased. Compared to the resting value, bicarbonate decreased in the A trial and this decrease was even more pronounced during the A + L trial. The P_{CO_2} was not different between the two trials. The venous plasma potassium reached 6.1 ± 0.2 and 7.0 ± 0.4 mM during the A and A + L trials, respectively. Plasma glucose did not change significantly but the venous concentration was always higher than the arterial concentration, i.e. there was a net glucose release from the arm during both trials.

The arterial plasma ionised calcium increased only marginally ($P = 0.18$) during the A trial, but the increase became significant during the A + L trial (Table 1). In venous blood, plasma calcium was increased from the resting value, but there was no significant difference between the two trials. Plasma calcium was higher in venous compared with arterial blood. Plasma sodium increased from 140 ± 0 at rest to 145 ± 1 mM during both exercise trials. The NA spillover increased 37-fold from rest to the A trial and thereafter almost doubled during the A + L trial (Fig. 2).

DISCUSSION

The major new finding of this study is that during combined arm and leg exercise, arm blood flow was about 20 % lower than during arm exercise alone. Our data demonstrate local vasoconstriction in the exercising arm during maximal whole body exercise to an extent that affects oxygen delivery to and utilisation by the working muscles.

During dynamic exercise the traditional view of metabolic muscle vasodilatation is that it eliminates the effect of the increased sympathetic activity and thereby serves for adequate regional perfusion. This model, termed 'functional sympatholysis' (Remensnyder *et al.* 1962) suggests that muscle blood flow is locally regulated by the release of substances (e.g. potassium) which directly or indirectly impede the α-sympathetic tone (Hansen *et al.* 2000). An increase in exercise intensity is associated with increased sympathetically mediated systemic vasoconstriction in internal organs including the splanchnic area (Perko *et al.* 1998). Furthermore, during dynamic exercise, sympathetic vasoconstriction, also occurring in active skeletal muscle, has been shown both in animals (O'Leary *et al.*1997; Buckwalter & Clifford, 1999) and in humans (Joyner *et al.* 1992). Therefore, it seems that the perfusion of contracting skeletal muscle is the result of a dynamic balance between metabolic vasodilatation, sympathetic vasoconstriction and the effect of the muscle pump. The net result of this dynamic balance seems to be partially dependent on the overall exercise intensity that results from multiple contracting muscles (Secher *et al.* 1977; Saito *et al.* 1992; Kagaya, 1993; Kagaya *et al.* 1994) as well as on the ability to increase cardiac output (Pawelczyk *et al.* 1992). During low intensity exercise oxygen delivery, by means of vaso-dilatation, is prioritised, while during intense whole body exercise, as is the case in the present study, blood pressure regulation, and therefore vasoconstriction, becomes of importance.

Previous studies that investigated the effect of adding arm to leg exercise on the leg blood flow have contrasting results (Secher *et al.* 1977; Savard *et al.* 1989; Richter *et al.* 1992; Richardson *et al.* 1995; Bangsbo *et al.* 1997). In fact, all but Secher's study have failed to demonstrate such vasoconstriction. One explanation for the discrepancy between these reports may be the choice of relative workloads shared between the arms and the legs during the exercise protocol. It is likely that the exercise protocol used

Figure 2. Catecholamines and noradrenaline spillover at rest and during arm (A) and combined arm and leg (A + L) exercise

Values are means ± S.E.M.; *n* = 10.
* Different from rest; + different from A, *P* < 0.05.

□ Adrenaline ■ Noradrenaline □ Noradrenaline spillover
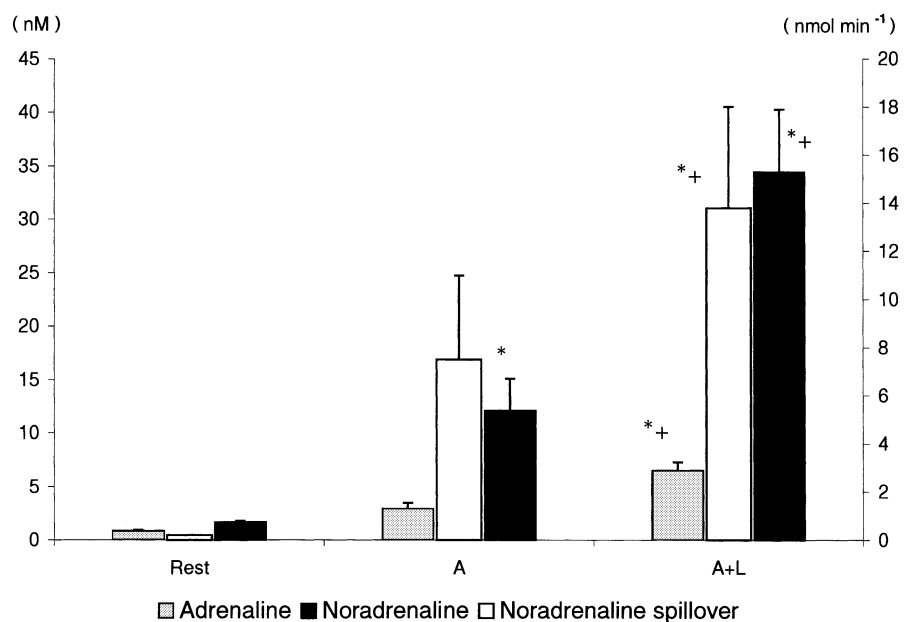
to investigate the effect of sympathetic vasoconstriction on the blood flow of active skeletal muscle should be strenuous enough to challenge the $\dot{Q}$ capacity, but not so intense that the exercise time is inadequate for the required measurements. During combined arm and leg exercise an elevated leg NA spillover was noted by Savard *et al.* (1989), Richter *et al.* (1992) and Richardson *et al.* (1995). From these data it can be argued that up to a given level, local vasodilatation is not overridden by sympathetic tone. It seems that net vasoconstriction ensues when the peripheral blood flow demand challenges the regulation of blood pressure, as demonstrated with an 8 % blood pressure reduction from the A to the A + L trial, in confirmation of data by Bevegård *et al.* (1966), Stenberg *et al.* (1967) and Secher *et al.* (1977).

Another explanation for the contrasting results amongst earlier studies may be the difference in experimental design and the lack of statistical power, due to a small sample size, to detect significant differences. Indeed, a meta-analysis of these studies including 32 subjects (Secher *et al.* 1977; Savard *et al.* 1989; Richter *et al.* 1992; Richardson *et al.* 1995; Bangsbo *et al.* 1997) revealed a mean effect size of 0.732 (95 % CI, 0.328–1.137) and a mean ± S.D. blood flow reduction of 11.0 ± 3.7%.

A decrease in flow with unchanged driving pressure would imply a decrease in arm vascular conductance. However, the 8 % reduction in MAP during the A + L trial suggests that the ~20 % reduction in arm blood flow cannot be attributed only to the sympathetic vasoconstriction but is also caused by the reduced driving pressure. On the other hand, support for a sympathetic influence on arm vascular conductance comes from a two-fold increase in noradrenaline spillover, which is an index of sympathetic nerve activity. During the A + L trial the lowered blood pressure observed in our study may have triggered the arterial baroreceptors that would have to either increase $\dot{Q}$ or reduce the vascular bed in order to restore the blood pressure to the set point established during arm exercise. Indeed, $\dot{Q}$ was increased by 68 % from the A trial to the A + L trial. However, increasing $\dot{Q}$ was not a sufficient response to restore blood pressure, and a reduction of the vascular bed by means of vasoconstriction appeared to be required. Furthermore, preliminary data from ongoing studies in our laboratory suggest that the baroreceptor operating point may be reset lower during the A + L compared to A exercise. This finding could explain the lower blood pressure observed during the A + L trial.

Two mechanisms have been suggested to govern blood pressure and elicit the net vasoconstriction and reduced blood flow that we observed in our study: (a) an influence from the central nervous system 'central command' (Querry *et al.* 2001) and (b) a muscle chemoreflex (Gallagher *et al.* 2001). Vasodilatation in active muscle facilitates oxygen delivery for the increasing metabolic demand, while vasoconstriction regulates arterial pressure. The arterial baroreceptor response through the sympathetic branches of the autonomic nervous system aims to return arterial pressure to the established central nervous system operating point (Raven *et al.* 2002). The outcome of the baroreceptor response is reflex tachycardia and systemic vasoconstriction. In our study, the vasoconstriction required for the maintenance of arterial pressure seems to override the vasodilatation needed for oxygen delivery and even ultimately for oxygen utilisation. These data support the notion that the arterial pressure is the primary regulated variable during whole body dynamic exercise.

Secher *et al.* (1977) showed reduced leg blood flow by addition of arm exercise even though the combined exercise intensity was only 77 % of $\dot{V}_{O_2,max}$, which seems unlikely to require a maximal $\dot{Q}$. The results showed, however, that leg blood flow was only reduced when the arm intensity (% of arm $\dot{V}_{O_2,max}$) exceeded 40 % of $\dot{V}_{O_2}$ during the combined exercise. Therefore, it is possible that vasoconstriction in the legs was effected due to the fatiguing workload imposed on the arms, without $\dot{Q}$ being maximal. Support for the existence of this mechanism comes from the studies of Saito *et al.* (1992), Kagaya (1993) and Kagaya *et al.* (1994) who reported a reduction in calf blood flow during fatiguing forearm contractions. In addition, Harms *et al.* (1997) reported that respiratory muscle fatigue can induce vasoconstriction in the exercising legs. Therefore, a second mechanism responsible for sympathetic excitation and vasoconstriction may be the muscle chemoreflex originating from type III and IV afferents stimulated by fatiguing muscle contractions (Harms *et al.* 1997).

The novelty of our findings is that the magnitude of the sympathetic tone was so high that it induced not only a reduction in flow but also in $\dot{V}_{O_2,arm}$. Even though oxygen extraction increased in the A + L trial, $\dot{V}_{O_2,arm}$ was not maintained due to the disproportionate reduction in blood flow. The effect of leg exercise on arm a–v O_2 difference has been reported by Secher *et al.* (1977) where an increase was seen only during intense leg exercise. In our study the 23 % increase in the arm oxygen extraction during the A + L trial (with ~60 % of work capacity) is in agreement with the previous data. The reduction in $\dot{V}_{O_2,arm}$ implies that ATP resynthesis from oxidative phosphorylation was impaired. Since power output was maintained constant, a proportionally greater reliance on non-oxidative ATP production might have occurred. The presumed increased energy contribution from anaerobic metabolism may have contributed to the increased lactate concentration in the venous blood during the A + L trial. However, the lactate (v–a) diff. suggests that the increase in arterial lactate concentration was not established by an increased lactate release from the arm muscles, which was lower, but possibly by a reduced lactate clearance from

other organs. Indeed, the legs release lactate during combined arm and leg exercise compared with a lactate clearance when the arms are working alone (Secher *et al.* 1977). Furthermore, with increased systemic vasoconstriction, hepato-splanchnic blood flow decreases and the contribution of the Cori cycle to glucose production is minimised (Nielsen *et al.* 2002). Therefore, a reduction in the lactate uptake by the liver may have also contributed to the accumulation of lactate in arterial blood. The decreased net lactate release may be explained by lactate uptake and partial utilisation of lactate as substrate. The increased arterial lactate concentration during the combined exercise possibly enhanced muscle lactate uptake by the arms as previously suggested (Richter *et al.* 1988) and decreased lactate release through a reduction of the muscle to blood lactate gradient as implicated by Richardson *et al.* (1995). The trend of the glucose (v–a) difference, which was almost halved during the A + L trial compared with the A trial, confirms a glucose release from contracting muscle at the onset of intense exercise (Jorfeldt & Wahren, 1970). The increase in ionised calcium, parallel to the drop in pH, reflects the increased calcium release from albumin and the depression of calcium reuptake by the sarcoplasmic reticulum (Byrd *et al.* 1989). The two-fold increase in NA spillover was apparently effective in countering the elevated, e.g. potassium-dependent, vasodilating stimulus and producing a net vasoconstriction in the working arm.

It should be mentioned that the combination of workloads used during the A + L trial may not be a 'realistic' way to distribute the effort between arms and legs during whole body exercise. The exercise protocol was meant to be a model for the demonstration of a physiological mechanism. It is most likely that whole body exercise is performed at a lower intensity for the arms and the legs, i.e. at an intensity that does not elicit a mutual reduction in flow.

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