NEURAL CONTROL OF CARDIOVASCULAR RESPONSES AND OF VENTILATION DURING DYNAMIC EXERCISE IN MAN

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SUMMARY

1. Nine subjects performed dynamic knee extension by voluntary muscle contractions and by evoked contractions with and without epidural anaesthesia. Four exercise bouts of 10 min each were performed: three of one-legged knee extension (10, 20 and 30 W) and one of two-legged knee extension at 2×20 W. Epidural anaesthesia was induced with 0·5 % bupivacaine or 2 % lidocaine. Presence of neural blockade was verified by cutaneous sensory anaesthesia below T8–T10 and complete paralysis of both legs.

2. Compared to voluntary exercise, control electrically induced exercise resulted in normal or enhanced cardiovascular, metabolic and ventilatory responses. However, during epidural anaesthesia the increase in blood pressure with exercise was abolished. Furthermore, the increases in heart rate, cardiac output and leg blood flow were reduced. In contrast, plasma catecholamines, leg glucose uptake and leg lactate release, arterial carbon dioxide tension and pulmonary ventilation were not affected. Arterial and venous plasma potassium concentrations became elevated but leg potassium release was not increased.

3. The results conform to the idea that a reflex originating in contracting muscle is essential for the normal blood pressure response to dynamic exercise, and that other neural, humoral and haemodynamic mechanisms cannot govern this response. However, control mechanisms other than central command and the exercise pressor reflex can influence heart rate, cardiac output, muscle blood flow and ventilation during dynamic exercise in man.

INTRODUCTION

During dynamic exercise cardiovascular responses and ventilation increase with the intensity of exercise. Evidence supports the concept that two neural mechanisms

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play a role in these responses. In one mechanism the neural activity responsible for the recruitment of motor units also activates the cardiovascular and respiratory control areas in the medulla and this has been termed central command (Johansson, 1895; Krogh & Lindhard, 1917; Mitchell & Schmidt, 1983). In the other mechanism, the neural activity caused by stimulation of mechano- and/or metaboreceptors in the contracting skeletal muscles activates these same control areas and this has been called the exercise pressor reflex (Alam & Smirk, 1937; Mitchell, Kaufman & Iwamoto, 1983). There appears to be redundancy between these two mechanisms and neural occlusion may be operative (Rybicki, Stremel, Iwamoto, Mitchell & Kaufman, 1989). However, during dynamic exercise the cardiovascular responses and ventilation may be regulated by other neural, humoral and haemodynamic mechanisms (Adams, Frankel, Garlick, Guz, Murphy & Semple, 1984).

We investigated cardiovascular, metabolic and ventilatory responses during dynamic exercise when both central command and the exercise pressor reflex were operative (voluntary exercise); when only the exercise pressor reflex was operative (electrically induced exercise) and when neither central command nor the exercise pressor reflex were operative (electrically induced exercise during complete epidural anaesthesia). This design allowed an assessment of the relative roles of central command and the exercise pressor reflex in determining cardiovascular and ventilatory responses to dynamic exercise. The effect of other neural, humoral and haemodynamic mechanisms were also evaluated when central command and the exercise pressor reflex were inoperative. A preliminary report of these findings has been presented (Strange et al. 1992).

METHODS

After informed consent twelve male subjects performed voluntary and electrically induced exercise in pilot experiments without catheters, but including placement of an arterial cuff on the lower leg. In no subject did the arterial cuff cause significant pain. However, in three subjects evoked exercise caused severe discomfort. Thus nine subjects, aged 21–32 years who tolerated evoked contractions well volunteered for the study which was approved by the Copenhagen and Karolinska ethical committees.

On the day of the main study, subjects came to the laboratory at 08.00 h and at least 2 h after a light breakfast catheters were inserted. After 30 min of rest, dynamic knee extension was performed with one or two legs on a modified electrically braked Krogh cycle ergometer (Andersen & Saltin, 1985). The subjects were placed with the upper body horizontal. A rod attached to the ankle and the crank of the ergometer was used to transfer movement of the lower leg to the cycle. The work rate was controlled by a weight balance system. Dynamic exercise was performed at a rate of sixty contractions per minute, with one contraction causing the lower leg to move from approximately 90 to 160 deg knee extension. After each contraction the flywheel momentum helped return the lower leg to the 90 deg starting position. An arterial cuff was placed just below the knee in order to insure that leg blood flow was representative of supply to the active muscles.

Voluntary muscle contractions

Subjects performed dynamic knee extensions for 4×10 min at an intensity of 10, 20, 30 W (one leg) and 2×20 W (two legs), with at least 10 min of rest between 30 W and 2×20 W. Pulmonary oxygen uptake was determined after 3 min of exercise at each work rate. Leg blood flow was measured twice at each exercise intensity. Between the two flow measurements, blood samples were taken simultaneously from the femoral artery and vein, and cardiac output was measured during the last 2 min of exercise.

Evoked muscle contractions

Knee extension was induced by muscle stimulation and subjects were instructed not to influence the evoked contractions. Otherwise the procedures were identical to those applied in the first part of the study. Dynamic knee extension was induced by a computer-controlled apparatus consisting of an arbitrary wave form generator (Kronhite 5920, USA) connected to an isolated battery powered amplifier (NASA, Biomedical Engineering, USA). Tenzcare (3M, USA) 76×114 mm electrodes were placed over vastus medialis just above the knee and proximally over vastus lateralis. A microswitch on the crank of the ergometer was activated when the pedal arm passed the horizontal position and triggered stimulation of the muscles. To induce contractions, a 50 Hz pulse train was applied with variable amplitude and duration (< 320 ms). A biphasic sine wave pulse shape was used because it delivers no net charge to the subject. It appeared that 0·5 ms was the optimal pulse width, because it induced sufficient contractions with minimal skin affection. The pulse amplitude was adjusted manually to maintain a kicking frequency of approximately 1 Hz. By a feedback loop from the Krogh cycle to the computer, the stimulus duration was automatically adjusted if the frequency changed.

Evoked muscle contractions and epidural anaesthesia

Epidural anaesthesia was induced, and the procedure from the second part of the study was repeated. Depending on the duration of the study, anaesthesia was maintained by a total dose of 25–50 ml 2 % lidocaine (two subjects) or 0·5 % bupivacaine (seven subjects) through a L3–L4 catheter. For the anaesthetic to become active 20–30 min was allowed. Presence of neural blockade was verified by cutaneous anaesthesia below T8–T10 and complete motor paralysis of both legs in all subjects. Full motor control of the legs was regained within 10 h of the last injection.

Measurements and calculations

Blood pressure was measured via a 20-gauge (1·0 mm) catheter inserted percutaneously into the right femoral artery and was recorded continuously from a Statham P23XL (USA) transducer placed at heart level. Mean arterial pressure was determined from the electronically filtered (1 Hz) pulsatile pressure (Simonsen & Weel Press 8041, Copenhagen, Denmark) and heart rate was derived from an electrocardiogram.

Cardiac output was determined by dye dilution (Dow, 1956). Five milligrams of indocyanine green (Cardio-Green, Becton & Dickinson, USA) in 2 ml of sterile water was injected via a centrally placed catheter inserted from a left cubital vein. Arterial blood was withdrawn at a rate of 20 ml min^{-1} (Harvard, model 2202A, USA). A densitometer cuvette (Waters Instruments, DC-410, USA) was placed between the catheter and the pump and connected to a cardiac output computer (Waters Instruments, CO-10, USA). The dye dilution curves were recorded on a Gould TA-2000 thermal array recorder, and withdrawn blood was reinfused. Calibration was performed after the experiment using blood samples with dye concentrations of 2·5 and 5 mg l^{-1}, respectively. Systemic vascular conductance was taken as the ratio of cardiac output to mean arterial pressure.

Leg blood flow was determined by the constant infusion thermodilution technique (Andersen & Saltin, 1985). A 12 cm Teflon 13-gauge (2·3 mm) catheter was inserted percutaneously in the right femoral vein with the tip advanced to a location approximately 2 cm above the inguinal ligament. A thermistor probe (Edslab probe 94-030-2·5F, USA) was inserted through the venous catheter and advanced 6–8 cm proximal to the catheter tip. Through four side holes, ice-cold saline was infused at a rate of 113 ml min^{-1} for 15–16 s. Temperature was recorded continuously by an Edslab Cardiac Output Computer 9520 (USA).

Leg vascular conductance was calculated as the average of the two leg blood flows divided by accompanying mean arterial pressure. Leg oxygen and glucose uptakes, as well as lactate and potassium releases were assessed from the average of the two flows and a single determination of arterial and femoral venous concentrations.

Haemoglobin content and oxygen saturation were measured on an OSM II Hemoxymeter (Radiometer, Copenhagen, Denmark). Blood oxygen and carbon dioxide tensions were determined on an ABL 30 analyzer (Radiometer) and plasma potassium on a Perkin-Elmer 372 atomic absorption spetrophotometer (Norwalk, CT, USA). Plasma lactate was assessed by a Yellow Springs Analyzer 23L (USA). Plasma adrenaline and noradrenaline were measured by high-performance liquid chromatography (Da Prada & Zürcher, 1976). Expired air was sampled in

Douglas bags and analysed for volume with a Tissot spirometer and for oxygen and carbon dioxide content by paramagnetic (Servomex) and infrared (Beckman LBL-II) apparatus, respectively.

Values in the text are means $\pm$ S.E.M. for rest and the average exercise response for all work rates except when otherwise stated. Friedman's two-way analysis of variance by rank was used to evaluate differences between the three experiments (Siegel & Castellan, 1988) and if proven significant, deviating results were located by Wilcoxon's signed ranks test. The level of significance was set to 0·05.

RESULTS

Blood pressure, heart rate and cardiac output

Rest

Mean arterial pressure was 96 ± 3 mmHg, and heart rate was 66 ± 4 beats min^{-1} before voluntary exercise, and these values were not significantly different before electrically induced exercise with or without epidural anaesthesia. Before and during epidural anaesthesia cardiac output ($6 \cdot 8 \pm 0 \cdot 4$ and $7 \cdot 8 \pm 0 \cdot 6$ l min^{-1}) and systemic vascular conductance (73 ± 5 and 85 ± 8 ml min^{-1} mmHg^{-1}) were similar (Fig. 1).

Exercise

Mean arterial pressure increased more during electrically induced exercise (to 112 ± 4 mmHg) than during voluntary exercise (to 103 ± 5 mmHg; $P < 0 \cdot 01$). However, during epidural anaesthesia the blood pressure response was absent at all exercise intensities (average value 89 ± 5 mmHg). Heart rate and cardiac output were lower during electrically induced exercise with epidural anaesthesia (85 ± 5 beats min^{-1} and 12 ± 1 l min^{-1}, respectively) than during control evoked exercise (91 ± 5 beats min^{-1} and 13 ± 1 l min^{-1}; $P < 0 \cdot 05$). Systemic vascular conductance was similar during the three exercise protocols.

Leg blood flow and oxygen uptake

Leg blood flow was not measured during rest. During control electrically induced exercise it increased more (to $3 \cdot 1 \pm 0 \cdot 1$ l min^{-1}) than during voluntary exercise (to $2 \cdot 3 \pm 0 \cdot 3$ l min^{-1}; $P < 0 \cdot 01$) and electrically induced exercise with epidural anaesthesia ($2 \cdot 6 \pm 0 \cdot 1$ l min^{-1}; $P < 0 \cdot 01$). During two-legged exercise (at 2×20 W), leg blood flow for one leg corresponded to the value obtained during one-legged exercise at 20 W. Compared to voluntary exercise (23 ± 2 ml min^{-1} mmHg^{-1}), leg vascular conductance increased more during electrically induced exercise (to 29 ± 1 ml min^{-1} mmHg^{-1}; $P < 0 \cdot 05$), both with and without epidural anaesthesia.

Leg oxygen uptake increased linearly with work rate during all three experiments and was higher during electrically induced exercise (320 ± 18 ml min^{-1}) compared to voluntary exercise (271 ± 21 ml min^{-1}; $P < 0 \cdot 05$) and exercise with epidural anaesthesia. During voluntary exercise and exercise with epidural anaesthesia, leg oxygen uptake was the same (Fig. 2).

Leg glucose uptake and lactate release

Leg glucose uptake was higher during electrical muscle stimulation with and without epidural anaesthesia than during voluntary exercise. During voluntary exercise blood lactate did not increase, while during evoked exercise with or without epidural anaesthesia a small increase was noted and lactate was released from the leg.
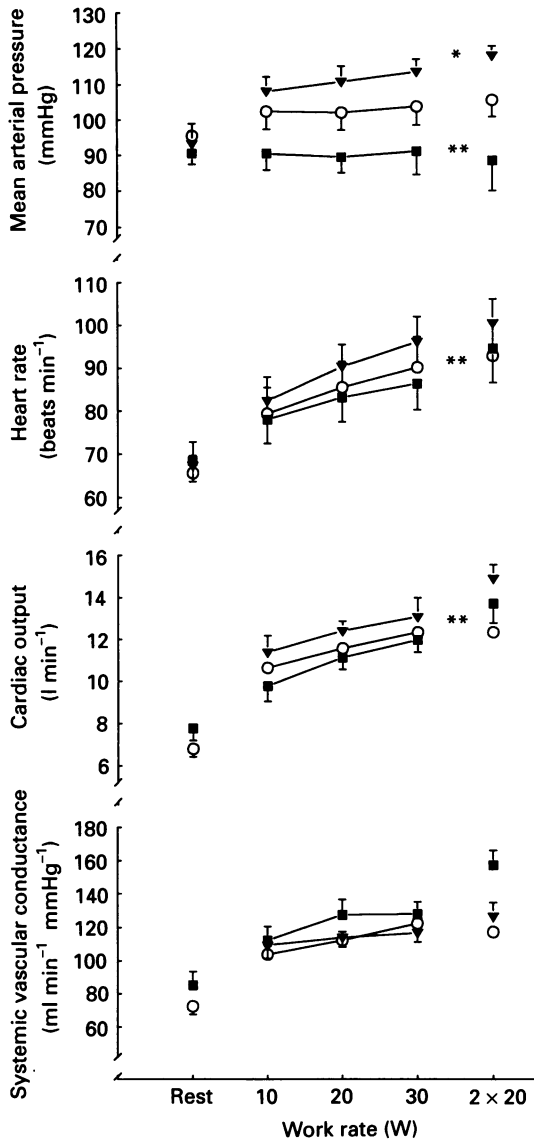
Fig. 1. Mean arterial pressure, heart rate, cardiac output and systemic vascular conductance at rest and during increased work rates. Work rates of 10, 20 and 30 W performed with one leg and 2×20 W performed with two legs. Values are means $\pm$ s.e.m. ($n = 9$) during voluntary dynamic exercise ($\bigcirc$), electrically induced dynamic exercise ($\blacktriangledown$) and with electrically induced dynamic exercise with epidural anaesthesia ($\blacksquare$). * Difference between voluntary and control electrically induced exercise. ** Difference between electrically induced exercise with and without epidural anaesthesia.

However, during 2×20 W exercise no lactate was released from the leg. Also arterial pH and bicarbonate remained at the resting levels during voluntary exercise, while they decreased during electrically induced exercise with and without epidural anaesthesia (Table 1).

Arterial oxygen tension increased during control electrically induced exercise. Femoral venous oxygen tension decreased during exercise. Arterial carbon dioxide tension decreased during evoked exercise with and without epidural anaesthesia, while the femoral venous values increased similarly during all types of exercise.
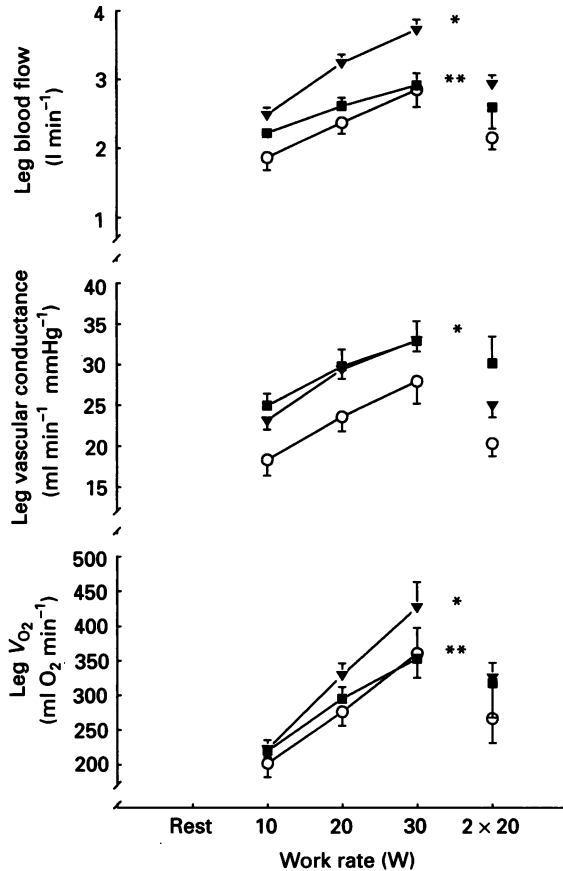

Fig. 2. Leg blood flow, leg vascular conductance and leg oxygen uptake (V_{O_2}) at increased work rates in watts. Symbols same as in Fig. 1.

Plasma potassium increased during all three types of exercise and was highest during electrically induced exercise with epidural anaesthesia. Thus, leg potassium release was larger during both types of evoked exercise. Plasma catecholamine levels did not change significantly.

Ventilation and oxygen uptake

Resting ventilation and pulmonary oxygen uptake were similar before voluntary and electrically induced exercise. During voluntary exercise ventilation increased linearly with the work intensity to a maximal value of 31 ± 5 l min^{-1} and there was no significant difference between the three exercise protocols. Pulmonary oxygen uptake was also similar. The largest oxygen uptake was 1.04 ± 0.06 l min^{-1} (Table 1).

DISCUSSION

This study demonstrated the importance of the exercise pressor reflex for the normal blood pressure response to dynamic exercise with a large muscle group in man. Epidural anaesthesia, which caused a profound sensory loss and complete motor paralysis of the legs, abolished the normal increase in blood pressure during

TABLE 1. Ventilation and cardiovascular responses

			Electrically induced exercise	
	Rest	Voluntary exercise	Control	Epidural anaesthesia
Ventilation (l min^{-1})	10.1 ± 1.2	19.7 ± 1.9*	21.4 ± 1.6*	19.4 ± 2.0*
Pulmonary V_{O_2} (l O_2 min^{-1})	0.36 ± 0.02	0.70 ± 0.05*	0.73 ± 0.04*	0.73 ± 0.05*
[Glucose]$_a$ (mmol l^{-1})	5.3 ± 0.3	4.7 ± 0.1*	4.7 ± 0.1	4.1 ± 0.1*†‡
[Glucose]$_v$ (mmol l^{-1})	5.0 ± 0.3	4.5 ± 0.1	4.5 ± 0.2	3.8 ± 0.2*†‡
Leg glucose uptake (mmol min^{-1})		0.4 ± 0.1	0.7 ± 0.1†	0.8 ± 0.1†
[Lactate]$_a$ (mmol l^{-1})	0.5 ± 0.03	0.6 ± 0.1	2.1 ± 0.1*†	1.7 ± 0.2*†
[Lactate]$_v$ (mmol l^{-1})	0.5 ± 0.04	0.7 ± 0.1	2.8 ± 0.2*†	2.3 ± 0.2*†
Leg lactate release (mmol min^{-1})		0.3 ± 0.09	2.1 ± 0.4†	2.0 ± 0.3†
pH$_a$	7.39 ± 0.00	7.39 ± 0.00	7.37 ± 0.00*†	7.36 ± 0.01*†
pH$_v$	7.36 ± 0.01	7.31 ± 0.01*	7.27 ± 0.01*†	7.26 ± 0.01*†
[HCO$_3^-$]$_a$ (mmol l^{-1})	24.6 ± 0.8	24.4 ± 0.8	22.4 ± 0.5*†	21.9 ± 0.7*†‡
[HCO$_3^-$]$_v$ (mmol l^{-1})	26.5 ± 0.8	28.6 ± 0.7*	26.2 ± 0.4†	26.0 ± 0.6†
Arterial P_{O_2} (mmHg)	101 ± 2	100 ± 2	108 ± 1*†	102 ± 1‡
Venous P_{O_2} (mmHg)	37 ± 2	24 ± 1*	29 ± 1*†	25 ± 2*‡
Arterial P_{CO_2} (mmHg)	42 ± 1	41 ± 1	39 ± 1*†	40 ± 1*†
Venous P_{CO_2} (mmHg)	48 ± 2	58 ± 2*	59 ± 2*	60 ± 2*
[K$^+$]$_a$ (mmol l^{-1})	3.8 ± 0.1	4.0 ± 0.1*	4.3 ± 0.1*†	4.5 ± 0.1*†‡
[K$^+$]$_v$ (mmol l^{-1})	3.9 ± 0.1	4.2 ± 0.1*	4.6 ± 0.1*†	4.9 ± 0.1*†‡
Leg K$^+$ release (mmol min^{-1})		0.2 ± 0.1	0.7 ± 0.2†	1.0 ± 0.2†
[Noradrenaline]$_a$ (nmol l^{-1})	0.71 ± 0.06	1.12 ± 0.12	1.30 ± 0.06	1.00 ± 0.18
[Noradrenaline]$_v$ (nmol l^{-1})	0.77 ± 0.06	1.06 ± 0.12	1.24 ± 0.12	0.95 ± 0.18
[Adrenaline]$_a$ (nmol l^{-1})	0.65 ± 0.22	0.71 ± 0.16	0.98 ± 0.38	0.71 ± 0.22
[Adrenaline]$_v$ (nmol l^{-1})	0.22 ± 0.05	0.55 ± 0.16	0.87 ± 0.32	0.55 ± 0.16

* Different from rest, $P < 0.05$. † Different from voluntary exercise, $P < 0.05$. ‡ Different from control electrically induced exercise, $P < 0.05$. a, arterial; v, venous sample.

dynamic leg exercise. This is in accordance with the findings by Kjær, Secher, Bach, Sheikh & Galbo (1989); Fernandes, Galbo, Kjær, Mitchell, Secher & Thomas (1990) and Hanel, Worm, Secher, Perko & Kjær (1992) of a reduced blood pressure response to voluntary dynamic leg exercise during epidural anaesthesia with 0·25 % bupivacaine. Friedman *et al.* (1993) found no effect on the cardiovascular responses to dynamic exercise during epidural anaesthesia with 1 % lidocaine. Together these findings demonstrate a dose-dependent attenuation of the blood pressure response to dynamic exercise with epidural anaesthesia. This may be interpreted to mean that blockade of the group III and/or IV muscle afferents needs to be almost complete in order to abolish the blood pressure response to dynamic exercise (Wilson, Wall, Matskawa & Mitchell, 1991).

Blood pressure, leg blood flow, oxygen and glucose uptakes and lactate release were larger during control evoked exercise than during voluntary exercise. However,

heart rate, cardiac output and ventilation were similar. These findings are in accordance with those of Krogh & Lindhard (1917); Asmussen, Nielsen & Wieth-Pedersen (1943); Adams, Garlick, Guz, Murphy & Semple (1984) and Adams, Guz, Innes & Murphy (1987). One concern is that evoked contractions are associated with direct stimulation of muscle afferents unrelated to the muscle contractions. However, in humans evoked contraction during partial neuromuscular blockade is associated with reduced heart rate and blood pressure responses (Iwamoto, Mitchell, Mizuno & Secher, 1987). Accordingly, in animal preparations the exercise pressor reflex is eliminated by neuromusclar blockade (Iwamoto *et al.* 1987; McMahon, McWilliam & Kaye, 1993).

A central role for reflex control of the circulation during dynamic exercise is demonstrated by the finding that blood pressure and heart rate are dominated by the absolute level of muscle activity. This is shown during dynamic exercise with partial neuromuscular blockade, when an increased effort at a given oxygen uptake does not significantly influence heart rate and blood pressure (Galbo, Kjær & Secher, 1987).

Also in agreement with the view that a reflex neural mechanism dominates the cardiovascular responses to dynamic exercise is the finding that occlusion of blood supply to muscle *after* exercise results in maintained blood pressure and, less consistently, heart rate (Alam & Smirk, 1937, 1938; Rowell, Hermansen & Blackmon, 1976; Freund, Rowell, Murphy, Hobbs & Butler, 1979; Fernandes *et al.* 1990). However, when blood pressure is maintained during postexercise muscle ischaemia, this effect is caused by a decrease in peripheral vascular conductance with rapidly decreasing cardiac output (Bonde-Petersen *et al.* 1978; Friedman *et al.* 1993). In contrast, *during* exercise blood pressure is elevated because cardiac output increases 'more' than peripheral conductance. Yet, a central finding from experiments with epidural anaesthesia is that when the pressor response to postexercise muscle ischaemia is affected, the blood pressure response to exercise is reduced (Fernandes *et al.* 1990). Conversely, when epidural anaesthesia does not affect the pressor response to postexercise muscle ischaemia, the pressor response to exercise is not diminished (Friedman *et al.* 1993).

A central neural mechanism for regulation of heart rate during dynamic exercise has been demonstrated only after training (Klausen, Secher, Clausen, Hartling & Trap-Jensen, 1982). When smaller muscle groups are activated as during one-legged exercise (Saltin, 1986; Innes, De Cort, Evans & Guz, 1992) and handgrip exercise (Jørgensen, Perko, Payne & Secher, 1993), central neural mechanisms may play an additional role.

The fact that central command is not required for the cardiovascular responses to dynamic exercise with large muscle groups is in contrast to what has been demonstrated during static leg exercise. During static exercise with neuromuscular blockade, the blood pressure and heart rate responses are enhanced (Leonard, Mitchell, Mizuno, Rube, Saltin & Secher, 1985; Victor, Pryor, Secher & Mitchell, 1989) and with a high level of partial curarization resulting in almost no force, the greatest responses are developed (Mitchell, Reeves, Rogers, Secher & Victor, 1989). Accordingly, after static exercise an arterial cuff does not maintain the exercise blood pressure (Leonard *et al.* 1985; Bull, Davies, Lind & White, 1989; Mitchell, Reeves, Rogers & Secher, 1989; Kjær, Secher, Bach, Galbo, Reeves & Mitchell, 1991).

The heart rate and cardiac output responses to dynamic leg exercise were only minimally affected by epidural anaesthesia. This could be due to baroreceptor mechanisms adjusting cardiac output to match the increased peripheral vascular conductance associated with muscle vasodilatation. Accordingly, Kjær *et al.* (1989), Fernandes *et al.* (1990) and Hanel *et al.* (1992), who also demonstrated a reduced blood pressure response to dynamic exercise during epidural anaesthesia, found no effect on the heart rate response. Thus, the lower blood pressure during electrically induced exercise with epidural anaesthesia would be expected to cause less baroreceptor inhibition (McMahon *et al.* 1993). Due to the possible interference of baroreceptor mechanisms, these types of experiments do not allow us to conclude that feedback from muscles is without importance for the heart rate response to dynamic exercise. It may be speculated that the muscle pump in the legs forms the primary motor to the circulation during electrically induced exercise, and that cardiac output becomes elevated following a Frank–Starling mechanism in response to an increased preload.

Blood flow to the exercising legs was reduced during epidural anaesthesia at all levels of exercise. This reduction was due only to the lower perfusion pressure, as the vascular conductance in the leg was unaffected. It is likely that the degree of epidural anaesthesia used in this experiment will block the sympathetic nerve activity to the legs (Lundin, Wallin & Elam, 1989; Rørdam, Jensen, Schroeder, Lorentzen & Secher, 1993). This is in contrast to the studies by Kjær *et al.* (1989), Fernandes *et al.* (1990) and Hanel *et al.* (1992) in which the sympathetic activity was probably not blocked because epidural anaesthesia extended only to the inguinal ligament. In this study plasma catecholamine levels were low and not significantly affected by epidural anaesthesia. Also, the fact that vascular conductance in the legs was unaffected by epidural anaesthesia indicates that sympathetic nerve activity to the legs does not control muscle vascular conductance during these levels of exercise. In addition, the lack of an increase in blood pressure during exercise with epidural anaesthesia was not due to a greater blood flow to the exercising muscle. It could also be speculated that the absence of a blood pressure response to exercise with epidural anaesthesia was a result of inability to reduce the splanchnic circulation. However, with the relatively modest increase in heart rate we established during exercise, the reduction in splanchnic blood flow would only be approximately 10% (Clausen & Trap-Jensen, 1974).

Compared to voluntary exercise, leg glucose uptake tended to be higher during electrical muscle stimulation with and without epidural anaesthesia. Arterial lactate levels and lactate release from the leg were also higher during electrical muscle stimulation despite a larger blood flow. This probably reflects a different pattern of muscle fibre recruitment and/or involvement of muscles. When exercise was performed with a large muscle mass, lactate was not released from the leg (Secher, Clausen, Klausen, Noer & Trap-Jensen, 1977; Richter, Kiens, Hargreaves & Kjær, 1992).

A normal ventilatory response to dynamic exercise occurred, when the central and reflex neural mechanisms were not operative. Similar findings were obtained with voluntary exercise during epidural anaesthesia with 0·25% bupivacaine (Kjæer *et al.* 1989; Fernandes *et al.* 1990; Hanel *et al.* 1992). Yet, intense 'activation' of central

command increases ventilation as demonstrated during exercise with partial neuromuscular blockade (Ochwadt, Bücherl, Kreuzer & Loeschke, 1959; Asmussen, Johansen, Jørgensen & Nielsen, 1965; Galbo *et al.* 1987). With this approach it should be noted that although ventilation, at any oxygen uptake, is larger during partial curarization, it decreases with work rate during increasing levels of neuromuscular blockade (Galbo *et al.* 1987). Accordingly, in patients with spinal cord injury, electrically induced exercise results in the normal ventilatory response (Adams *et al.* 1984). Humoral mechanisms, such as carbon dioxide and potassium (McCoy & Hargreaves, 1992), may dominate ventilation during dynamic exercise and other mechanisms have only a modulating influence. In this study the effect of a decrease in carbon dioxide tension during evoked contractions may have been outbalanced by an increase in plasma potassium and a decrease in pH.

While a normal or elevated blood pressure response occurs during electrically induced exercise (central command not operative), blood pressure does not increase during electrically induced exercise with epidural anaesthesia (central command and the exercise pressor reflex not operative). Thus, the exercise pressor reflex is essential for the normal blood pressure response to dynamic exercise and other neural, humoral and haemodynamic mechanisms cannot govern this response. However, control mechanisms other than central command and the exercise pressor reflex can influence heart rate, cardiac output, muscle blood flow and ventilation during dynamic exercise in man.

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