Research Paper

Clinical Autonomic Research 3, 21–30 (1993)

Vascular and electromyographic responses evoked in forearm muscle by isometric contraction of the contralateral forearm

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THERE is controversy over whether isometric contraction of the forearm evokes vasoconstriction or vasodilatation in the muscles of the contralateral forearm. In the present study we have investigated in normal man, the effects of isometric contraction of one arm at 75, 50 and 25% maximum voluntary contraction (MVC) on arterial pressure, heart rate, blood flow and vascular resistance of the contralateral forearm and on electromyographic (EMG) activity recorded from that same arm with sensitive, surface electrodes.

When EMG activity was not being recorded from the 'resting' arm, isometric contraction of the contralateral arm for 2 min evoked increases in arterial pressure and heart rate whose magnitudes were graded with % MVC and an increase in forearm blood flow and a decrease in forearm vascular resistance at 75, 50 and 25% MVC, indicating vasodilatation. Further experiments in which EMG activity was recorded from the 'resting' arm demonstrated that the decrease in forearm vascular resistance evoked by 75% MVC was associated with a substantial increase in EMG activity of the extensor and flexor muscles of that arm. By contrast, when forearm contraction was performed at 75% MVC whilst subjects viewed the EMG activity in the 'resting' arm on an oscilloscope and kept EMG activity minimal, vascular resistance increased in that arm, indicating vasoconstriction. Further, when subjects performed contraction at 25% MVC whilst showing minimal EMG activity in the contralateral arm, vascular resistance in that same arm increased (from 78 ± 16 to 124 ± 29 mmHg/ml/min/100 ml tissue). These results are discussed in relation to those of previous studies. We propose, that in normal man, isometric contraction of the forearm evokes primary vasoconstriction in the muscles of the contralateral forearm, but that this response may be overcome by muscle vasodilatation occurring secondary to unintended muscle contraction or as part of the alerting response to acute stress.

Key words: Isometric exercise, Cardiovascular reflexes muscle blood flow

Introduction

There is substantial evidence that in normal human subjects isometric contraction of the forearm evokes vasoconstriction in the kidney, splanchnic circulation[1] and in the cutaneous circulation of various parts of the body, including the skin of the contralateral forearm[2]. However, the responses evoked in the skeletal muscles of the contralateral forearm are equivocal, controversy centring over whether they show vasodilatation or vasoconstriction.

Lind *et al.*,[3] who recorded electromyographic (EMG) activity in the flexor muscles of the forearms and blood flow in that same region by using venous occlusion plethysmography, reported that forearm blood flow sometimes increased during isometric contraction of the contralateral arm, but only if the 'resting' arm showed EMG activity. This increase in blood flow was attributed to vasodilatation in skeletal muscle mediated by vasodilator metabolites released as a consequence of unintended muscle contraction. It was proposed that when there was no EMG activity, the muscles showed vasoconstriction, so explaining the lack of change in blood flow in the face of a rise in arterial pressure. However, Lind *et al.*[3] did not calculate the forearm vascular resistance, even though they had the arterial pressure measurements that would allow them to do this. If this is done then it appears that all four subjects who took part in the study actually showed an increase in vascular resistance in the 'resting' forearm, indicating vasoconstriction, irrespective of whether EMG activity was increased.

Lind *et al.*[4] used later studies to substantiate their own proposals. In a first series of experiments, each subject performed weak isometric contractions (1–10% maximum voluntary contraction, MVC)

with the arm that was going to be the 'resting' arm in a second series of experiments. Blood flow was recorded from that arm and a linear correlation, or 'calibration' curve was obtained between EMG activity and blood flow. When, in the second series of experiments, contraction was carried out with the contralateral arm at 33 and 40% MVC, Lind *et al.*[4] reported that six out of twelve subjects showed an increase in blood flow in the 'resting' forearm, and an associated increase in EMG activity and that these values fitted well on the 'calibration' curve. Thus, they concluded that the increase in forearm blood flow reflected muscle vasodilatation whose magnitude was directly related to the force of contraction. However, since arterial pressure was not measured, such a conclusion was not justified. Indeed, since the increases in arterial pressure evoked by 1–10% MVC would have been much smaller than those evoked by 33 and 40% MVC and since muscle blood flow is directly dependent on arterial pressure, as well as indirectly dependent on muscle vascular resistance, it is rather surprising that the results obtained in the second series of experiments did fall on the 'calibration' curve obtained in the first series.

By contrast, Eklund *et al.*[5] who carried out similar experiments, but calculated forearm vascular resistance, reported that there was a decrease in forearm vascular resistance during the first minute of isometric contraction of the contralateral arm which waned slightly during the second minute. They also reported that if EMG activity increased in the 'resting' arm it did so in the second, but not in the first, minute of isometric contraction and therefore discounted unintended muscle contraction as a cause of the vasodilatation. Later experiments involving α- and β-adrenoreceptor blockade led to the conclusion that the vasodilatation was due to an increase in sympathetic nerve activity, the noradrenaline released acting on post-junctional β-adrenoreceptors.[6] Rusch *et al.*[7] made similar observations to Eklund *et al.*,[5] but proposed that the muscle vasodilatation was mediated by activation of sympathetic cholinergic fibres. If this were the case then this implies that the muscle vasodilatation was part of the alerting response to acute emotional stress,[8] rather than a response to isometric contraction *per se*.

In view of these uncertainties, we have carried out further experiments on the effect of isometric contraction of the forearm on the vasculature of the contralateral forearm. We measured arterial pressure so that vascular resistance could be calculated and recorded EMG activity using two pairs of sensitive surface electrodes[9] which were arranged so that they should effectively record electrical activity in the mass of flexor and extensor muscles of the forearm. For comparison we also recorded vascular responses in the calf. Some of these results have been presented to the Physiological Society.[10]

Methods

Experiments were performed on healthy human subjects who were volunteers from the academic, research and technical staff of the Department of Physiology and undergraduates. Each subject sat on a couch with their legs horizontal and the torso inclined at 45° to the legs, in a quiet room maintained at 21–23°C. All recording devices were positioned behind the subject so as to minimize visual and auditory stimuli, except in Protocol 3, see below.

Isometric handgrip was carried out with the left hand by gripping a modified inflated cuff of a sphygmomanometer. At the beginning of each experiment, 100% MVC was determined as described previously.[2] Arterial pressure was recorded from the contralateral forearm using a semi-automatic sphygmomanometer, the output of which was displayed on a pen recorder. An ECG was recorded via standard limb leads and was used to obtain heart rate which was displayed continuously on the pen recorder. Respiration was monitored continuously via a stethograph. All of these techniques have been described in detail previously.[2]

In the experiments of Protocols 2 and 3 (see below) a second sphygmomanometer cuff was placed around the left wrist. This was inflated to 200 mmHg to exclude the circulation to the hand during the measurement of forearm blood flow by venous occlusion plethysmography.[11] For the latter purpose, a mercury-in-silastic strain gauge was fastened around the forearm at the region of largest circumference. The arm was supported with foam cushions so that it lay in a horizontal position 4–5 cm below the heart, as measured from the fifth rib. The output from the strain gauge and wheatstone bridge circuit was recorded on the pen recorder. Blood flow was calculated in ml per 100 ml of tissue per min.[11,12]

In the experiments of Protocol 4, blood flow was recorded from the right calf (i.e. contralateral to the forearm contraction) as just described, except that cuffs were placed around the ankle to allow occlusion of the circulation to the foot, and around the thigh; the strain gauge was placed around the calf at the region of its largest circumference. The calf was supported so that it was 10–12 cm below the heart.

In the experiments of Protocol 3, EMG recordings were made from the right forearm using two pairs of surface electrodes similar in design to those described by Johnson *et al.*[9] Each electrode (1 cm diameter) together with a pre-amplifier was

incorporated into a compact araldite encasement of approximately 3 × 4.5 × 1 cm, the preamplifier being supplied with a 12 volt supply from a separate unit. One pair of electrodes was arranged 1 cm apart and 5 cm distal to the medial condyle of the elbow joint and the other pair was arranged 1 cm apart, 5 cm distal to the lateral condyle so that they recorded respectively from the major flexor and extensor muscles of the forearm. In each case the area of skin under the electrode was cleaned with surgical spirit, conducting gel was used to ensure good contact and the electrode was fixed to the site with double-sided adhesive tape. The outputs from the electrode pairs were connected to the two channels of an oscilloscope (Tetronix 225). Permanent records of EMG activity were taken using a camera (Polaroid Shackman 7000).

In each experiment a measurement of arterial pressure was taken as soon as the sphygmomanometer cuff had been placed on the right arm. Measurements were taken at regular intervals while the remaining recording apparatus was fitted to the subject and until a stable reading was obtained. Each subject equilibrated to the experimental room and apparatus for at least 30 min before the experiment began.

Protocols

1. Repetition of hand grip: These experiments were performed on eleven subjects (seven female, four male) aged 22.4 ± 1.5 years (mean ± SEM). Each subject performed two, 2-min periods of handgrip of the left hand at 75% MVC separated by a 5-min rest period. Arterial pressure was recorded at the end of the second minute of each period of contraction, and at 1-min intervals during the rest period. After a further 5-min rest period, the subject carried out two 2-min periods of contraction at 50% MVC, followed by two, 2-min periods of contraction at 25% MVC, each period of contraction being followed by a 5-min rest period. Arterial pressure was recorded at intervals as described for 75% MVC.

2. Vascular responses in the contralateral forearm: These experiments were carried out on 15 subjects (seven female and eight male), aged 23.1 ± 2.0 years.

Following the equilibration period 3 or 4 recordings were made at 1–2 min intervals of arterial pressure and forearm blood flow by using venous occlusion plethysmography. Each measurement of blood flow was made immediately (< 30 s) before the corresponding measurement of arterial pressure, so that the values could be used to calculate forearm vascular resistance (see below). Heart rate was noted at the same times.

The subject then performed two isometric contractions at 75, 50 and 25% MVC as described in Protocol 1. In the first contraction of each pair, arterial pressure and heart rate were recorded at the end of the first and second minutes, while in the second contraction of each pair, forearm blood flow and heart rate were recorded at the end of the first and second minutes. During the rest periods all variables were recorded at 1-min intervals as described in Protocol 1.

3. EMG activity in the contralateral forearm: These experiments were carried out on six subjects (three female, three male) aged 22.0 ± 1.9 years.

Two 2-min periods of contraction were peformed at 75% MVC as described in Protocol 2, whilst EMG activity was being continuously monitored. The oscilloscope was out of view of the subject; permanent records of EMG activity were taken during the rest period and during the second minute of contraction. In three of the subjects this was repeated for a third pair of contractions at 75% MVC, but this time each subject was asked to watch his/her EMG activity on the oscilloscope and endeavour to keep it to a minimum.

All six subjects carried out two further 2-min periods of contraction at 25% MVC just as described for 75% MVC as well, whilst EMG activity was being recorded out of their view.

4. Vascular responses in the contralateral calf: These experiments were carried out on 13 subjects (five female, eight male) aged 20.8 ± 1.0 years, exactly as described in Protocol 2 except that calf blood flow was recorded instead of forearm blood flow.

As a respiratory gasp, Valsalva manoeuvre or other abdomino-thoracic straining movements can evoke cardiovascular changes,[1] the subjects were asked to avoid such movements during and after contraction. In all of the experiments reported here, neither the respiratory recording, nor visual inspection revealed any evidence of such movement. In fact, respiration became more regular, deeper and faster during contraction (see Ref. 2).

Some subjects who took part in Protocols 2, 3 and 4 were unable to sustain 75% MVC for a full 2 min. In these cases, measurements made at the end of the first minute of contraction are presented below.

Forearm and calf vascular resistance were calculated by dividing mean arterial pressure in mmHg by the corresponding measurement of forearm and calf blood flow and expressed in ml/min/100 ml.

Statistical analyses: Control values for each variable were obtained by calculating the mean of the three measurements made before each period of contraction. Differences between control values and those

recorded during isometric hand grip were tested using Student's paired t-test: $p < 0.05$ was taken as significant.

Results

Protocol 1: Mean arterial pressure increased significantly from the resting value by the end of the second minute of contraction at 75, 50 and 25% MVC (see Fig. 1). These changes were graded with the force of contraction. As can be seen from Fig. 1, arterial pressure returned to the original control level between periods of contraction. The values of arterial pressure recorded at the end of the second minute of the first and second period of contraction were not significantly different at any force of contraction (see Fig. 1).

Protocol 2: These experiments showed that mean arterial pressure and heart rate were increased significantly both at the first and second minutes of contraction at 75, 50 and 25% MVC. The changes tended to be greater at the second than at the first minute and they were graded with the force of contraction (Fig. 2). Concomitantly there were increases in mean blood flow in the forearm contralateral to the isometric contraction to extents that were graded with the force of contraction at both the first and second minutes of contraction, although some individuals showed no change or a decrease in blood flow. Meanwhile, forearm vascular resistance generally decreased, indicating vasodilatation. These changes also seemed to be graded with force of contraction in that the changes reached significance at the first and second minutes of contraction at 75% MVC, at the first but not the second minute of contraction at 50% MVC and not at all during contraction at 25% MVC. In fact, at the second minute of contraction at 50% MVC, nine of the 15 subjects showed a decrease but six showed a decrease in forearm vascular resistance, while during contraction at 50 and 25% MVC, ten and seven subjects showed a decrease, but the remainder showed an increase in forearm vascular resistance. All variables returned to the initial control values during the rest periods.

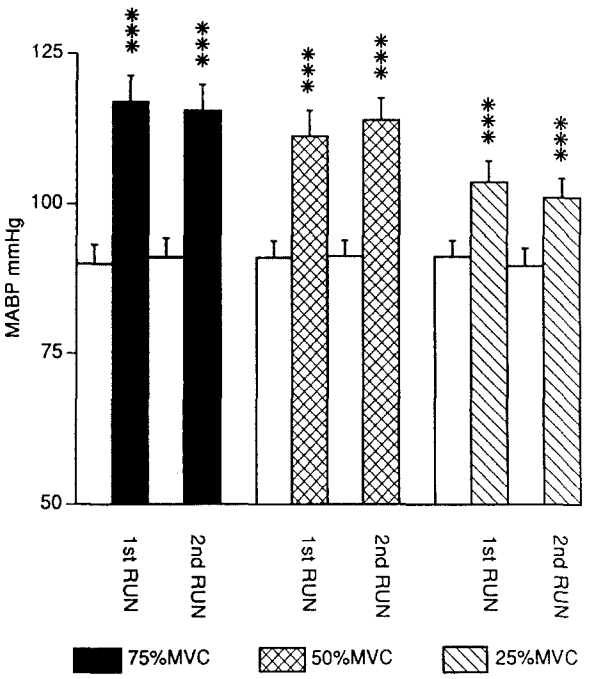

FIG. 1. Effect of repetition of isometric hand-grip at 75, 50 and 25% MVC on arterial pressure (MABP). Each column represents mean ± SEM, $n = 11$. Open columns indicate values recorded at the end of 5-min rest period, shaded columns indicate values recorded at the end of the second minute of isometric contraction at 75, 50 and 25% MVC as indicated below columns. ***$p < 0.001$; **$p < 0.01$; *$p < 0.05$.

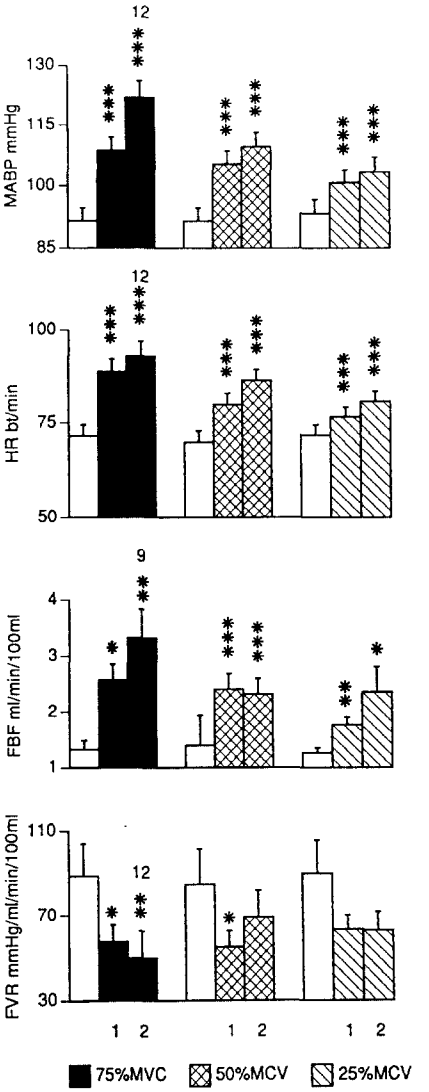

FIG 2. Changes evoked in arterial pressure, heart rate and in forearm blood flow and forearm vascular resistance by isometric contraction of the contralateral arm at 75, 50 and 25% MVC. From above, downward, mean arterial pressure (MABP) in mmHg recorded from the right arm, heart rate (HR) in beats/min, forearm blood flow (FBF) recorded from the right arm in ml/min/100 ml tissue, forearm vascular resistance (FVR) in mmHg/ml/min/100 ml tissue. Each column represents mean ± SEM. Open columns indicate values recorded at the end of 5-min rest period, shaded columns indicate values successively recorded at the end of the first and second minutes of isometric contraction of the left arm at 75, 50 and 25% MVC as indicated below. Significant difference from control indicated as in Fig. 1; $n = 15$ except when indicated otherwise by numbers above columns.

Protocol 3: In these experiments, only one of the six subjects was able to maintain contraction at 75% MVC for 2 min, but at the end of the first minute of contraction there were increases in arterial pressure and forearm blood flow and a decrease in forearm vascular resistance that were fully comparable to those recorded in Protocol 2 (Fig. 3A). During the rest periods, when the subject was asked to relax the right arm, i.e. the one contralateral to the handgrip, negligible EMG activity was recorded from both flexor and extensor muscles in that arm (see Fig. 4). However, during contraction of the left arm at 75% MVC, all subjects showed a large increase in EMG activity in the right arm, the increase in the extensors generally being greater than in the flexors (Fig. 4). Furthermore, in the one subject who managed to maintain contraction with the left arm at 75% MVC, for the full 2 min, blood flow in the right forearm increased from 1.5 to 2.52 ml/min/100 ml at the first minute and increased further to 14.28 ml/min/100 ml at the second minute, forearm vascular resistance being decreased progressively from 66.7 to 47.6 to 9.7 mmHg/ml/min/100 ml tissue at the first and second minutes respectively, indicating progressive vasodilatation. In association with these vascular changes the EMG activity in the right arm was far more pronounced at the second minute than at the first minute.

When three of these subjects were asked to perform a third period of contraction at 75% MVC with the left arm whilst viewing their own EMG activity in the right arm and keeping it to a minimum, one subject was unable to maintain low EMG activity and the blood flow in his right arm increased from 1.1 to 1.7 ml/min/100 ml, while vascular resistance decreased from 98.1 to 91.4 mmHg/ml/min/100 ml. By contrast, the other two subjects successfully maintained a low level EMG activity in the right arm that was not obviously different from that seen during the rest periods and in both cases their right forearm blood flow decreased and their forearm vascular resistance increased (see Fig. 5).

In the six subjects who performed 2-min contraction at 25% MVC with the left arm without being able to view their own EMG activity, arterial pressure increased by the end of the second minute as in the other protocols (Fig. 3B). However, in contrast to Protocol 2, there was a tendency for mean blood flow in the right forearm to decrease; this did not reach significance because some subjects showed an increase in blood flow. Moreover, in contrast to Protocol 2, forearm vascular resistance showed a significant and substantial increase, indicating vasoconstriction. In these subjects, four showed no detectable increase in EMG activity in the right forearm, while two showed a slight increase.

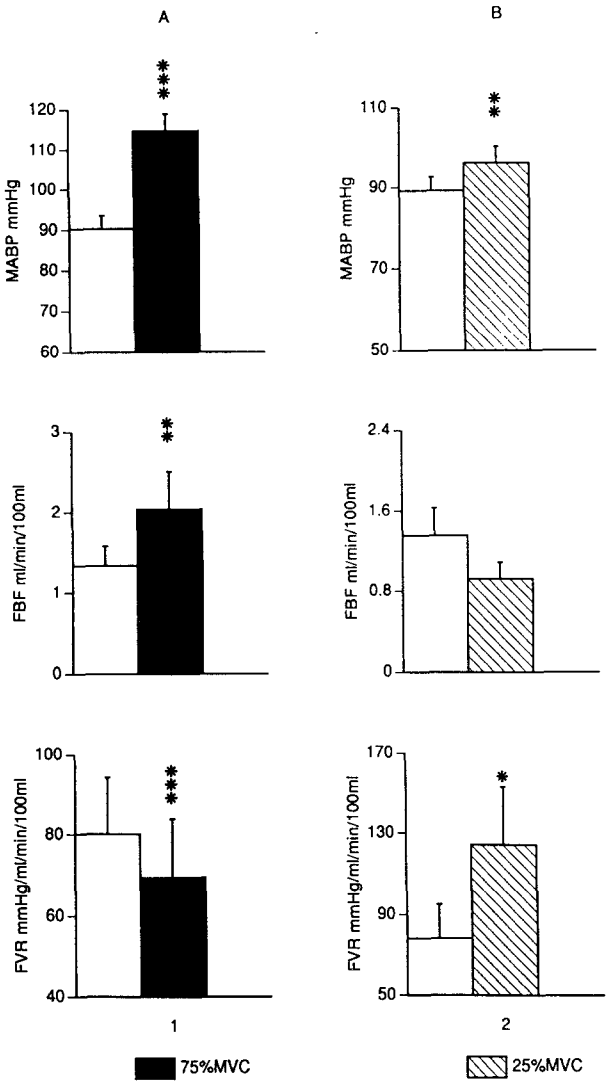

FIG. 3. Changes evoked in arterial pressure, forearm blood flow and forearm vascular resistance by isometric contraction of the contralateral arm at 75% MVC (A) and 25% MVC (B), whilst EMG was being recorded from the 'resting' forearm. Abbreviations and symbols as in Fig. 2. Open columns indicate mean values ± SEM recorded at the end of 5-min rest period, shaded columns indicate mean values ± SEM recorded at the end of the first minute of contraction at 75% MVC (A), and at the end of the second minute of contraction at 25% MVC (B), $n = 6$ in both A and B.

Protocol 4: In these experiments the changes recorded in arterial pressure and heart rate were fully comparable to those recorded in Protocols 1–3 (Fig. 6). Calf blood flow showed no significant change except at the second minute of contractions at 25% MVC when it was significantly decreased. At other times, the trend was for calf blood flow to decrease, except at the first minute of 75% MVC (Fig. 6). In association with these changes, calf vascular resistance tended to increase, indicating vasoconstriction, this reaching significance at the first and second minutes of 50% MVC and at the second minute of 25% MVC. There were, however, some subjects who showed a decrease in calf vascular resistance, particularly at 75% MVC: some of these commented that they had contracted their

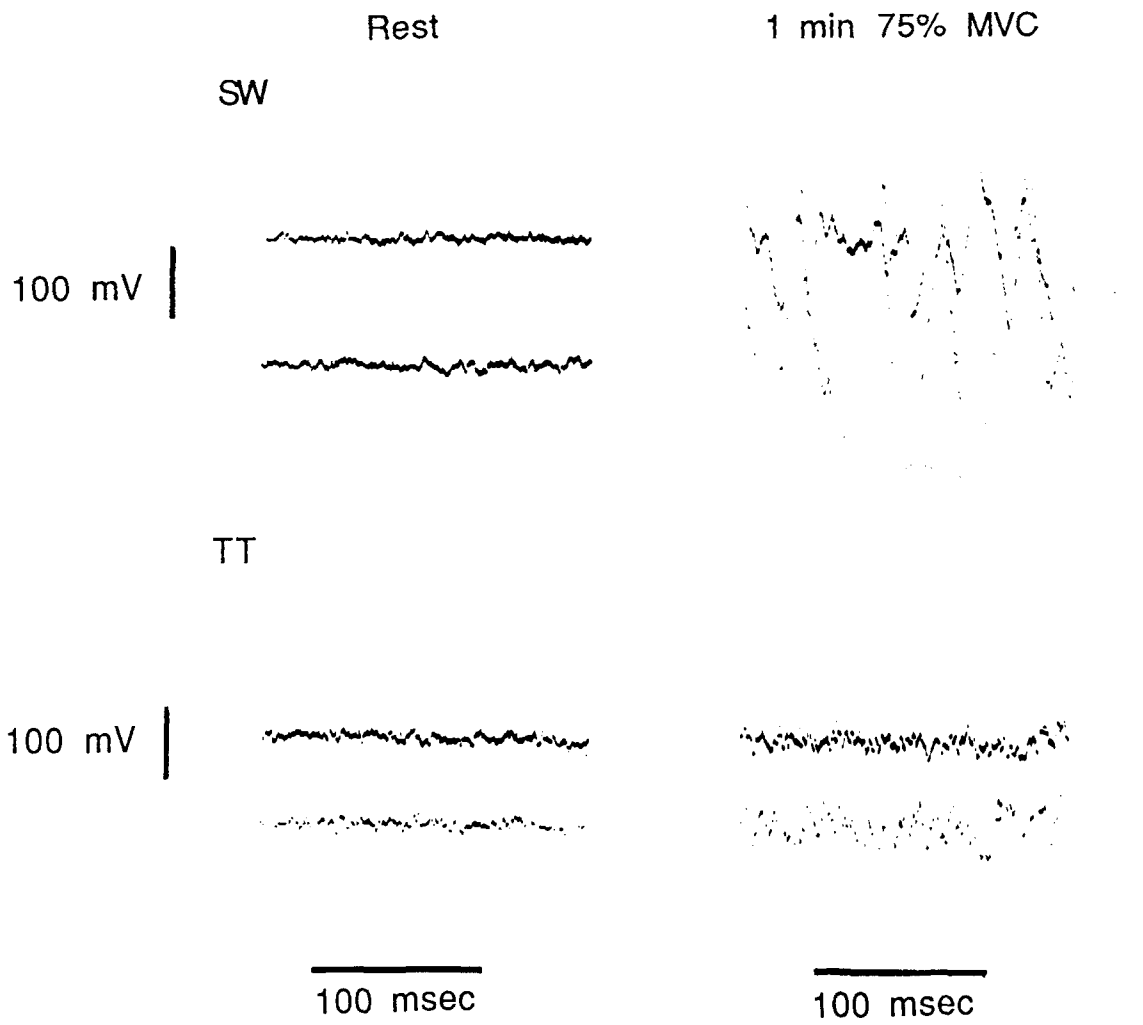

FIG. 4. Electromyographic activity recorded from the right arm during rest period (LHS) and at the end of the first minute of contraction of the left arm at 75% MVC (RHS). The recordings were taken from two different subjects (above and below) during the experiments shown in Fig. 3A. In each pair of recordings, the upper trace was recorded from the flexor muscles and the lower trace, from the extensor muscles.

calf muscles whilst striving to maintain the forearm contraction. We observed that some subjects dorsiflexed their toes during some contractions, this being particularly obvious at 75% MVC.

Discussion

In the present study, isometric contraction of one forearm for 2-min periods evoked increases in arterial pressure and heart rate that were graded with the force of contraction and during each period of contraction both variables increased progressively from the first to the second minute of contraction. These results are fully consistent with those reported in many other studies (see Ref. 1, for review). Further, the experiments of Protocol 1 showed that the increases in arterial pressure evoked by a given force of contraction were consistent on repetition as has been reported before.[1] Thus, it was justifiable in Protocols 2,3 and 4 to use the measurement of arterial pressure taken in one experimental run and the measurement of blood flow taken in a second experimental run to calculate regional vascular resistance. In the experiments of Protocol 2, isometric contraction evoked an increase in contralateral forearm blood flow at least in some subjects in broad agreement with the results of previous studies.[3–7] Moreover the fact that this was accompanied by a decrease in forearm vascular resistance, indicating net vasodilatation, is consistent with the results of Eklund *et al.*,[5,6] Rusch *et al.*[7] and Duprez *et al.*[13] The important issue, in view of the controversy in the literature (see Introduction), is whether the forearm vasodilatation reflected functional hyperaemia in skeletal muscle secondary to unintended contraction of those muscles as proposed by Lind *et al.*[3,4] or whether it was neurally mediated as deduced by Eklund *et al.*,[5,6] Rusch *et al.*[7] and Duprez *et al.*[13]

First, it should be stated that in recent experiments involving a very similar protocol to those of the present study, we demonstrated that

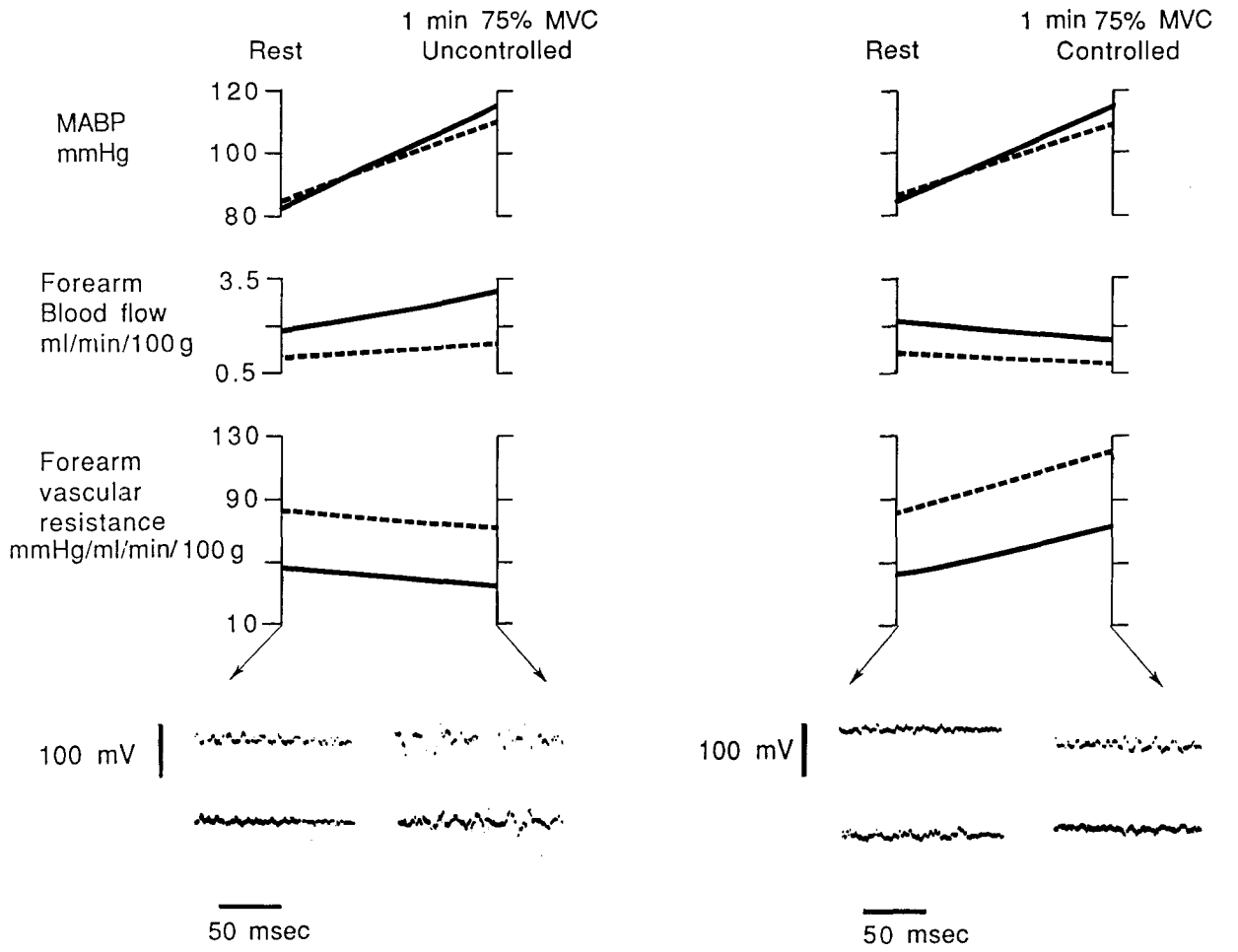

FIG. 5. Effects of isometric contraction of the left arm at 75% MVC on arterial pressure, forearm blood flow and vascular resistance recorded from the right arm and on EMG activity recorded from the right arm when the subjects did not (LHS) and when they did (RHS) attempt to control their own EMG activity (see text). Diagrams above show values recorded from two different subjects at rest and at the end of the first minute of contraction at 75% MVC, connected by continuous or dashed lines. EMG recordings below were taken from one of those subjects at corresponding times. Each pair of EMG recordings were taken from flexor muscles (above) and extensor muscles (below).

graded forces of isometric contraction of the forearm produced graded vasoconstriction the cutaneous circulation of the contralateral forearm.[2] Thus, it is reasonable to conclude that the decrease in forearm vascular resistance we recorded in the present study was due to vasodilataton in muscle, rather than in skin.

In the experiments of Protocol 3, when EMG activity was recorded, there was a remarkably close relationship between the EMG activity in the arm contralateral to the isometric hand grip and the change in vascular resistance in that arm. Firstly, all the subjects showed a clear increase in EMG activity during contraction at 75% MVC, when they made no attempt to keep EMG activity to a minimum and these subjects showed a significant decrease in forearm vascular resistance. Moreover, the one subject who managed to maintain 75% MVC for 2 min showed a clear, further increase in EMG activity from the first to the second minute and a corresponding further decrease in vascular resistance. Secondly, when two subjects managed to carry out a second period of 75% MVC with minimal EMG activity, the decrease in forearm vascular resistance that had been seen in the first period of contraction when there was substantial EMG activity, was reversed to an increase in vascular resistance during the second period. On the other hand, the third subject, who was unable to maintain a low level of EMG activity, showed a substantial decrease in forearm vascular resistance during both contractions.

The simplest explanation for these results would be that the decrease in forearm vascular resistance reflected muscle vasodilatation secondary to unintended muscle contraction in the 'resting' forearm as proposed by Lind *et al.*[3,4] and that the increase in forearm vascular resistance reflected vasoconstriction in muscle as well as skin, as part of the primary response to isometric exercise. The latter is consistent with the gradual increase in muscle sympathetic activity that has been recorded in the lower limbs during isometric contraction of the forearm.[14,15] Moreover, the disparity between the results of Protocol 2 when contraction at 25% MVC evoked a decrease in forearm vascular and those of

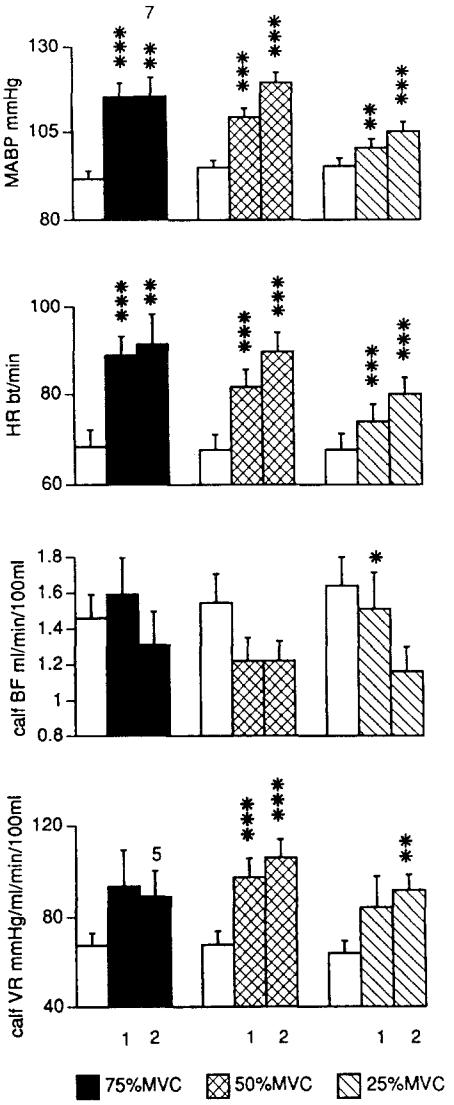

FIG. 6. Changes evoked in arterial pressure, heart rate and in calf blood flow and calf vascular resistance by isometric contraction of the contralateral arm at 75, 50 and 25% MVC. Abbreviations, symbols and columns as in Fig. 2 except that two bottom rows show calf blood flow (calf BF) and calf vascular resistance (calf VR), $n = 13$.

Protocol 3 when contraction at 25% MVC evoked an increase in forearm vascular resistance can be explained in a manner that is consistent with this explanation. For, although the subjects were not told the precise reasons for the experiments performed, they all had some knowledge of physiology and knew what each item of recording equipment was being used for. Thus, it was easy for them to deduce that in Protocol 3 we were checking whether or not the 'resting' arm was at rest. It is therefore not surprising that we recorded little EMG activity in these experiments. By contrast, in Protocol 2, when there was no check, it is likely that there was unintended contraction of the resting arm and a consequent metabolic dilatation.

Although these results accord well the proposal of Lind *et al.*[3,4] on the link between vasodilatation in forearm muscle and unintended muscle contraction, they do not accord fully with the results on which their proposal was based. They reported that when EMG activity increased, forearm blood flow always increased, whereas in our experiments blood flow generally increased, but sometimes did not change and sometimes fell. There is no obvious reason for this disparity. In our study, the clear relationship was between an increase in EMG activity and a decrease in the vascular resistance of the forearm, which is exactly what would be expected, given that blood flow is a dependent variable which is determined by arterial pressure and vascular resistance. Further, Lind *et al.*[3,4] reported that when there was no increase in EMG activity, forearm blood flow did not change whereas in our study (see Fig. 3B) blood flow generally fell under these conditions. There is no obvious reason for this disparity either; in our experiments the vasoconstriction in the forearm must have been greater in relation to the increase in arterial pressure than was the case in the experiments of Lind *et al.*[3,4]

In the studies which led to the opposing view, that forearm vasodilatation observed during isometric contraction of the contralateral forearm is neurally mediated, this conclusion was based primarily on the fact that no increase in EMG activity was recorded in the resting arm during the first minute of isometric contraction when the vasodilatation reached its peak. In the experiments of Eklund *et al.*,[5,6] EMG activity was recorded with needle electrodes which were inserted at unspecified sites in the forearm muscles. These necessarily sample from a localized site, whereas surface electrodes, such as we used, can record electrical activity from a large mass of muscle tissue. Thus, it is possible that electrical activity did occur during the first minute but it was missed by their recording system. This view is supported by the observation of Eklund *et al.*[5] that during voluntary contraction of the arm, EMG activity had to increase eight to ten times above the resting level before any increase in blood flow in that arm could be recorded. If this activity had been recorded from a large mass of muscle, rather than from a localized site, then an increase in muscle blood flow should have been recorded during much smaller changes in EMG activity, given that muscle arterioles are so sensitive to vasodilator metabolites released on muscle contraction that even a single muscle twitch can cause their dilatation (see Ref. 16). Rusch *et al.*[7] and Duprez *et al.*[13] who supported the findings of Eklund *et al.*,[5,6] used surface electrodes to record EMG activity, but gave no details of the sensitivity of the recording apparatus and provided no information on the recordings made. Thus, it is possible that they too missed evidence of muscle activity in the 'resting' arm.

However, if for the sake of argument we accept the conclusions of these various groups that the resting arm was indeed at rest, then we should consider the mechanisms proposed for neurally mediated vasodilatation and whether or not they contributed in our study: Eklund and Kaijser,[6] believing that isometric contraction evokes an increase in sympathetic noradrenergic activity to skeletal muscle as has been shown by several groups,[14,15,17] discounted the possibility that the forearm vasodilatation they recorded was mediated by inhibition of sympathetic noradrenergic fibre activity. This left two obvious possibilities, (i) activation of sympathetic cholinergic fibres, and (ii) stimulation of β-adrenoreceptors. They favoured the latter since the forearm vasodilatation was found to be reduced by the β-adrenoreceptor antagonist propranolol.[6] However, in view of evidence that adrenaline leveles in blood only increase slightly during isometric contraction and not until the second minute,[18] they concluded that the dilatation was not mediated by circulating adrenaline, but by noradrenaline which was released from sympathetic nerve terminals and which acted on post-junctional β-adrenoreceptors as had been demonstrated in the dog.[19] Rusch *et al.*[7] argued against this possibility since neurally mediated β-adrenoreceptor stimulation could not be demonstrated in man (see Ref. 20). Instead they favoured activation of sympathetic cholinergic fibres. This they supported with their observation that while isometric contraction produced dilatation in the contralateral forearm, it produced vasoconstriction in the calf, just as occurs in response to the acute emotional stress of mental arithmetic.[7] Sympathetic cholinergic fibres to muscle are known to be specifically activated only during the alerting or defence response to acute emotional stress in cats and dogs[8] and they have been similarly implicated, together with circulating adrenaline, in the vasodilatation that occurs in the forearm of human subjects in response to mental arithmetic.[21]

More recently, Mark *et al.*[22] reported that isometric contraction of one forearm evoked a *decrease* in muscle sympathetic activity recorded from the peroneal nerve. They concluded that this represented 'central command' the effect that the forebrain is thought to exert on vasomotor neurones during volitional exercise,[1] despite the substantial evidence that if central command plays a role at all, it tends to increase sympathetic vasoconstrictor fibre activity.[1,23,24] It was this conclusion that led Duprez *et al.*[13] to propose that the forearm vasodilatation they recorded during isometric contraction of the contralateral arm was due to inhibition of sympathetic vasoconstrictor fibre activity caused by increased central 'command'.

But, these conflicting ideas may be incorporated into a single hypothesis; that isometric contraction of the forearm can evoke vasodilatation in the contralateral forearm muscles as part of the alerting or defence response. As indicated above, the muscle vasodilatation of this response has been attributed to activation of sympathetic cholinergic fibres and the action of circulating adrenaline on β-adrenoreceptors in man[21] as well as in cats and dogs,[8] while evidence from experiments on cats has indicated that it is due in part to inhibition of sympathetic noradrenergic fibre activity.[25] Whether or not the alerting response is evoked in any particular study on isometric contraction would depend on the emotional state of the individual and the number of times the stimulus had been applied, since the muscle vasodilatation of the alerting response habituates on repetition,[8] as well as on the emotional stress imposed by the experimental equipment and experimenter. In the present study, we may have avoided evoking an alerting response because each subject was habituated to the experimental room and recording techniques during the equilibration period before the experiment proper began. Indeed, if we had evoked the alerting response, we would have expected it to have been most obvious when we imposed additional emotional stress by asking the subject to perform isometric contraction whilst maintaining minimal EMG activity in the contralateral arm. Yet this was the very condition in which we saw substantial vasoconstriction in the forearm.

Thus, having reviewed the evidence we believe we have provided firm evidence for the proposal put forward by Lind *et al.* (see Ref. 1) that the primary reponse evoked in the muscles of the forearm by isometric contraction of the contralateral forearm is vasoconstriction. But we suggest that this response may be overcome by secondary vasodilatation occurring as a local metabolic response to unintended muscle contraction, or as part of the alerting response to emotional stress.

This proposal is also appropriate for the vascular responses evoked in the calf. In agreement with other studies, we found that calf vascular resistance generally increased progressively from the first to the second minute of forearm contraction[5,7,13] as can be explained by a progressive increase in the activity of the sympathetic fibres that supply calf muscles.[14,15] Vasodilatation occurring in calf muscles as part of the alerting response may be less likely than in forearm muscles.[7] However, given the perception of individual subjects that they unintentionally contracted their calf muscles, together, our observations of dorsiflexion of the toes and the fact that these subjects tended to show a decrease in calf vascular resistance, it seems primary vasoconstriction evoked in the calf by isometric contraction of

the forearm can also be masked by metabolic vasodilatation secondary to intended muscle contraction.

References

1. Lind AR. Cardiovascular adjustments to isometric contraction: static effect. In: Shepherd JT, Abboud FM, eds. *Handbook of Physiology*, Section 2 Vol II, pt 2. Bethesda, MD: Am Phys Soc, 1983: 916–947.
2. Cotzias C, Marshall JM. Differential effects of isometric exercise on the cutaneous circulation of different regions. *Clin Auton Res* 1992; **2**: 235–241.
3. Lind AR, Taylor SH, Humphreys PW, Kennelly BM, Donald KW. Circulatory effects of sustained voluntary muscle contraction. *Clin Sci* 1964; **27**: 229–244.
4. Lind AR, Dahms TE, Williams CA, Petrosky JS. The blood flow through the 'resting' arm during hand-grip contractions. *Circ Res* 1981; **48** (Suppl I): 104–109.
5. Eklund B, Kaijser L, Knutsson E. Blood flow in resting (contralateral) arm and leg during isometric contraction. *J Physiol* 1974; **240**: 111–124.
6. Eklund B, Kaijser L. Effect of regional α- and β-adrenergic blockade on blood flow in the resting forearm during contralateral isometric hand grip. *J Physiol* 1976; **262**: 39–50.
7. Rusch NJ, Shepherd JT, Webb RC, Vanhoutte PM. Differential behaviour of resistance vessels of human calf and forearm during contralateral isometric exercise, mental stress and abnormal respiratory movements. *Cir Res* 1981; **48** (Suppl I): 118–130.
8. Hilton SM. The defence-arousal system and its relevance for circulatory and respiratory control. *J Exp Biol* 1982; **100**: 159–174.
9. Johnson SW, Lynn PA Miller S, Reed GAL. A skin-mounted pre-amplifier for recording the surface electromyogram. *J Physiol* 1977; **269**: 16P.
10. Cotzias C, Marshall JM. Vascular responses evoked by isometric hand-grip in the contralateral forearm of human subjects. *J Physiol* 1991; **438**: 93P.
11. Whitney RJ. The measurement of volume changes in human limbs. *J Physiol* 1953; **121**: 1–27.
12. Holling HE, Boland HC, Russ E. Investigation of arterial obstruction using a mercury-in-rubber strain gauge. *Am Heart J* 1962; **62**: 194–205.
13. Duprez DA, Essandoh LK, Vanhoutte PM, Shepherd JT. Vascular responses in forearm and calf to contralateral static exercises. *J Appl Physiol* 1989; **66**: 669–674.
14. Saito M, Naito M, Mano T. Different responses in skin and muscle sympathetic nerve activity to static muscle contraction. *J Appl Physiol* 1990; **69**: 2085–2090.
15. Seals DR. Sympathetic neural discharge and vascular resistance during exercise in humans. *J Appl Physiol* 1989; **66**: 2472–2478.
16. Marshall JM, Tandon HC. Direct observations of muscle arterioles and venules following contraction of skeletal muscle fibres in the rat. *J Physiol* 1984; **350**: 447–459.
17. Delius W, Hagbarth A, Hongell A, Wallin BG. Manoeuvres affecting sympathetic outflow in human muscle nerves. *Acta Physiol Scand* 1972; **84**: 82–94.
18. Kozlowsky S, Brzezinska Z, Nazar K, Kowalski W, Franczyk M. Plasma catecholamines during sustained isometric exercise. *Clin Sci* 1973; **45**: 723–731.
19. Viveros OH, Garlick DG, Renkin EM. Sympathetic beta adrenergic vasodilatation in skeletal muscle of the dog. *Am J Physiol* 1968; **215**: 1218–1225.
20. Brick I, Hutchinson KJ, Roddie IC. The effect of beta-adrenergic receptor blockade on the vasodilator response in the forearm to voluntary hyperventilation. *J Physiol* 1966; **187**: 645–649.
21. Barcroft H, Brod J, Hejl Z, Hirzjarvic EA, Kitchin AH. The mechanism of the vasodilatation in the forearm muscle during stress (mental arithmetic). *Clin Sci* 1960; **19**: 577–586.
22. Mark AL, Victor RG, Herhed C, Wallin BG. Microneurographic studies of the mechanisms of sympathetic nerve responses to static exercise in humans. *Cir Res* 1985; **57**: 461–469.
23. Goodwin GM, McCloskey PI, Mitchell JH. Cardiovascular and respiratory responses to changes in central command during isometric exercise at constant muscle tension. *J Physiol* 1972; **226**: 173–190.
24. Mitchell JH, Schibye B, Payne FC, Altin B. Response of arterial pressure to static exercise in relation to muscle mass, force development and electromyographic activity. *Circ Res* 1981; **48** (Suppl I): 70–75.
25. Dean C, Coote JH. Discharge patterns in postganglionic neurones to skeletal muscle and kidney during activation of the hypothalamic and midbrain defence areas in the cat. *Brain Res* 1986; **377**: 271–278.

Received 3 December 1992; accepted 30 December 1992.