Journal of Physiology (1989), **417**, *pp.* 13–24
With 4 text-figures
Printed in Great Britain

EPIDURAL ANAESTHESIA AND CARDIOVASCULAR RESPONSES TO STATIC EXERCISE IN MAN

BY J. H. MITCHELL*, D. R. REEVES JR*, H. B. ROGERS*
AND N. H. SECHER

From the Department of Anaesthesia, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, DK-2100 Copenhagen Ø, Denmark

(*Received 6 January 1989*)

SUMMARY

1. In human subjects, sustained static contractions of the knee extensors were performed in one leg with the same absolute (10% of the initial maximal voluntary contraction) and relative (30% of the maximal voluntary contraction immediately prior to the static exercise) intensities before and during epidural anaesthesia. Epidural anaesthesia reduced strength to 62 ± 8% of the control value and partially blocked sensory input from the working muscles. During contractions performed with the same relative force, the increases in mean arterial pressure and heart rate were greater during control contractions than during epidural anaesthesia. During contractions at the same absolute force, there was no significant difference in magnitude of cardiovascular responses between control contractions and contractions performed during epidural anaesthesia.

2. The metabolic role in the exercise pressor reflex was assessed by applying an arterial leg cuff 10 s before cessation of exercise and through the following 3 min of recovery. Although mean arterial pressure and heart rate decreased immediately after cessation of exercise, application of the arterial occlusion cuff resulted in higher post-exercise mean arterial pressure and heart rate values. Control and epidural mean arterial pressures during arterial occlusion were not significantly different.

3. The results of this study suggest that the reflex neural mechanism rather than the intended effort (central command) is important in determining the blood pressure and heart rate responses to static exercise in man. That is, when epidural anaesthesia diminishes sensory feedback and produces muscular weakness, central command does not determine the cardiovascular response. This conclusion, however, is opposite to that derived from experiments with partial neuromuscular blockade which demonstrated the importance of central command in determining the cardiovascular response to static exercise (Leonard, Mitchell, Mizuno, Rube, Saltin & Secher, 1985). Taken together, these two studies are complementary and support the concept that both central and reflex neural mechanisms play roles in regulating arterial blood pressure and heart rate during static exercise in man.

* Present address: The Harry S. Moss Heart Center, U. T. Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, TX 75235-9034, USA.

MS 7454

INTRODUCTION

A reflex neural mechanism (feedback control) as well as a central neural mechanism (feedforward control called 'central command') may generate the increases in heart rate and mean arterial blood pressure that are part of the cardiovascular responses to static exercise (Mitchell & Schmidt, 1983; Mitchell, 1985). Partial sensory nervous blockade, by means of epidural anaesthesia, should attenuate or eliminate the reflex originating in working muscles which has been termed the 'exercise pressor reflex' (Mitchell, Kaufman & Iwamoto, 1983), allowing an evaluation of the role of the reflex neural mechanism in determining the cardiovascular response to static exercise.

Using this model during dynamic exercise in man normal ventilatory and heart rate responses, but less of an increase in mean arterial pressure, have been found during submaximal and maximal exercise (Hornbein, Sørensen & Parks, 1969; Kjær, Secher, Fernandes, Galbo, Thomas & Mitchell, 1988). Furthermore, reversible post-exercise ischaemia of dynamically exercising muscle maintains mean arterial pressure, heart rate, and ventilation (Alam & Smirk, 1937, 1938) which are attenuated by epidural anaesthesia (Freund, Rowell, Murphy, Hobbs & Butler, 1979; Kjær *et al.* 1988).

Sensory blockade during static exercise in man has been performed only with brief isometric contractions (Freund *et al.* 1979; Lassen, Mitchell, Reeves, Rogers & Secher, 1989). With the use of partial neuromuscular blockade during sustained static contractions, an important role for central command in the regulation of mean arterial pressure and heart rate in man has been suggested (Leonard *et al.* 1985; Victor, Pryor, Mitchell & Secher, 1989; Mitchell, Reeves, Rogers, Secher & Victor, 1989).

We have studied static one-leg knee extension during epidural anaesthesia to determine if reflexes from the working muscles also participate in the cardiovascular response to static exercise. The model used was similar to that previously applied during static exercise with partial neuromuscular blockade (Leonard *et al.* 1985). Epidural anaesthesia was employed to reduce muscle strength to approximately 60% of control strength as well as to block sensory feedback from the contracting muscle. During epidural anaesthesia, the same absolute force was maintained as during the control study to emphasize the role of central command. That is, during epidural anaesthesia, the reduced muscle strength requires the subject to try harder (greater central command) to maintain the same absolute force as developed during the control study. Conversely, the maintenance of the same relative force as during the control study allows central command to be held constant. In other words, during epidural anaesthesia, even though the absolute developed force was reduced, the subject must exert the same effort to hold the same percentage of his present maximal voluntary contraction as he held during the control study.

METHODS

Nine healthy volunteers (six male; three female) were studied. Their mean age was 28 years (range 21–48 years), weight was 75 kg (range 58–89 kg), and height was 180 cm (range 170–190 cm).

All subjects were informed of the risks involved with participation in the experiment before they gave their verbal consent. The study was approved by the Municipal Ethical Committee of Copenhagen.

At the start of the experiment, a polyethylene catheter was placed in a superficial hand vein for isotonic saline infusion. A second catheter was inserted into the left brachial artery and connected

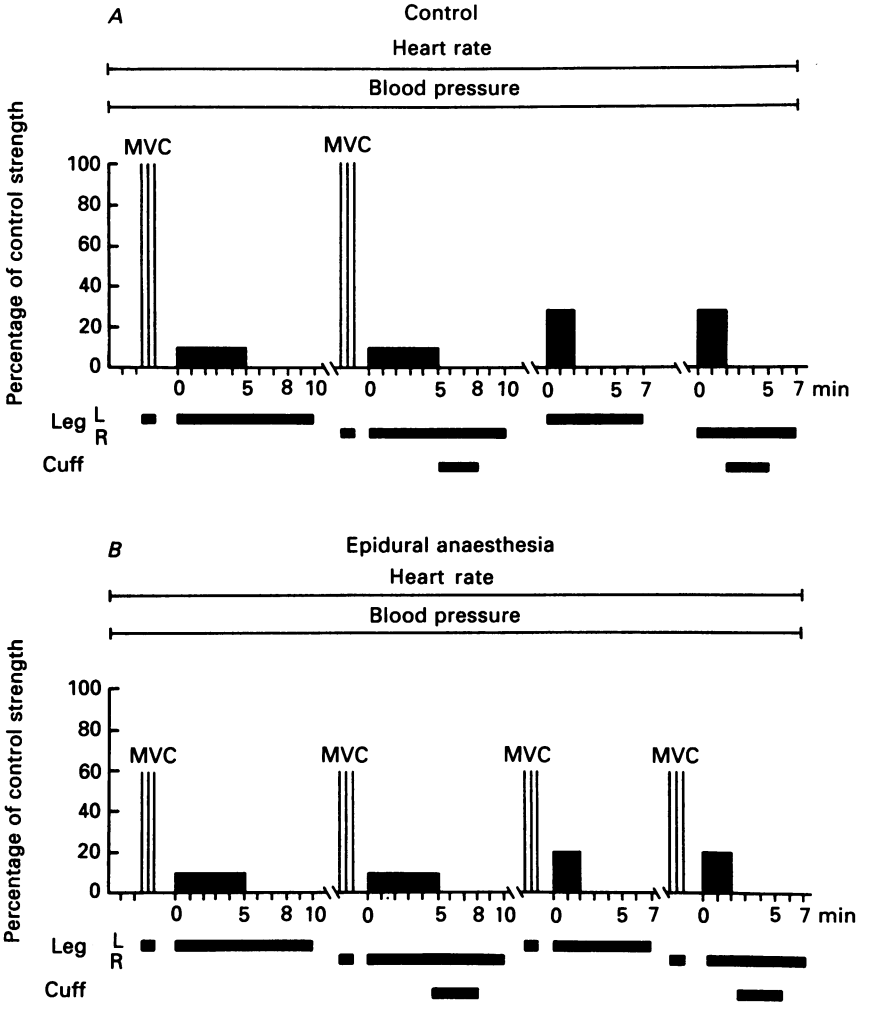

Fig. 1. Schematic diagram of the experimental protocol.

to a pressure transducer positioned at heart level in the semi-supine position. The electrocardiogram was taken from bipolar electrodes applied to the chest. Respiratory rate was monitored by a strain-gauge pneumograph connected around the chest. All variables were continuously monitored before, during, and after static contractions on a Siemens-Elema recorder.

Static muscle contractions were performed using the knee extensors (quadriceps femoris muscles) with the subject semi-supine and the lower leg vertical (knee angle, 90 deg). The force was determined with a circular strain-gauge applied just above the ankle. Results were calculated as a torque (N m).

At the beginning of the experiment and before each epidural exercise period, the strength of each

leg was established with three maximal voluntary contractions (MVC), the greatest of which was taken as the strength of that leg (Fig. 1). Each leg then performed a sequence of four contractions maintained either for 5 min at the same absolute force (10% of initial MVC) or for 2 min at the same relative force (30% of MVC immediately prior to static exercise). All control contractions were performed prior to their corresponding contractions after epidural anaesthesia (Fig. 1). The sequence was randomized, however, with respect to type of contraction and presence of cuff. Care was taken to avoid pressure or stretch of the sciatic nerve, thereby preventing paresthesias in the experimental leg. Respiratory excursions were continuously monitored to ensure that the subjects did not inadvertently perform a Valsalva manoeuvre. Whenever the subjects tended to hold their breath, they were instructed to breathe normally. Immediately after each sustained contraction, the intensity of effort was quantified by the rating of perceived exertion (Borg, 1970). In this rating, '7' represents very, very light, '13' means somewhat hard, and '19' signifies very, very hard.

Lidocaine (Xylocain, Astra) (seven subjects: 18–24 ml, 2% or 16–25 ml, 1%) or bupivacain (Marcain, Astra) (two subjects: 22 or 27 ml, 0·25%), was administered epidurally through intervertebral space L3–L4 employing a 20-gauge spinal needle and the 'loss of resistance' technique. Approximately 3/4 l of physiological saline was administered to each subject. The level of anaesthesia was established by using light touch by either the subject or one of the investigators. A more extensive neurological examination of both legs was performed in two subjects in order to determine the type and degree of sensory loss. Position sense was determined by moving the big toe and having the subject guess its position (i.e. dorsiflexion). Vibration sense was determined by placing a vibrating tuning fork upon the patella and sole of the foot. A cotton ball run along the leg determined light touch sensation. Sharp and deep pain were evaluated by pin pricking and squeezing the Achilles tendon, respectively. Temperature sensation was determined by alternately placing heated and cooled sides of a tuning fork against the leg. Finally, maximal voluntary contractions of the knee extensors were repeated to determine the degree of motor weakness.

In half of the sustained contractions, circulatory occlusion was established with a 20 cm wide pneumatic pressure cuff placed proximally on the thigh and inflated to 400 mmHg 10 s before the end of exercise. The cuff remained inflated for the following 3 min of recovery. The final recorded value after a further 2 min rest represented the end of recovery.

The analysis is based on mean arterial pressure and heart rate data collected over time. The data were collected on the nine subjects every 30 s for 10 and 7 min at the same absolute and relative work loads, respectively (Fig. 1). The effect of epidural anaesthesia was compared to a control and the presence of a cuff was compared to no cuff for all time periods. The exercise period began at zero time and recovery began at 5 and 2 min for the same absolute and relative work loads, respectively. For the same absolute work load, times zero, 30 s, 2 min and 5 min were included in the model while times 5·5, 6, 6·5, 7, 7·5 and 8 min comprised the recovery data. The same relative work load exercise data included times zero, 30 s, 1 and 2 min. The recovery data for this work load were times 2·5, 3, 3·5, 4, 4·5 and 5 min. Respiratory rates for all subjects were measured at rest, during the exercise period, and at the end of exercise.

Variables are presented as mean values $\pm$S.E.M. The data were evaluated using repeated measures analysis of variance on two different models. The first model tested for effects of epidural anaesthesia and time and of any interaction during static exercise. A second similar model, used for recovery, included the cuff effect in addition to the effects of epidural anaesthesia and time. Pairwise comparisons of each level of significant effects were made using Dunn's t test. A P value of 0·05 was considered significant. Paired t tests were employed to analyse the differences in respiratory rates.

RESULTS

The average strength of one-leg knee extension was 211 ± 22 N m and no significant difference existed between the values obtained with the right and left leg. The average leg strength under epidural anaesthesia was 62 ± 8% of control, and the usual level of anaesthesia was 5 cm below the umbilicus. In two subjects with similar levels of cutaneous paresthesia as the other subjects in the study, a more extensive neurological examination was performed on both legs. In this examination, it was

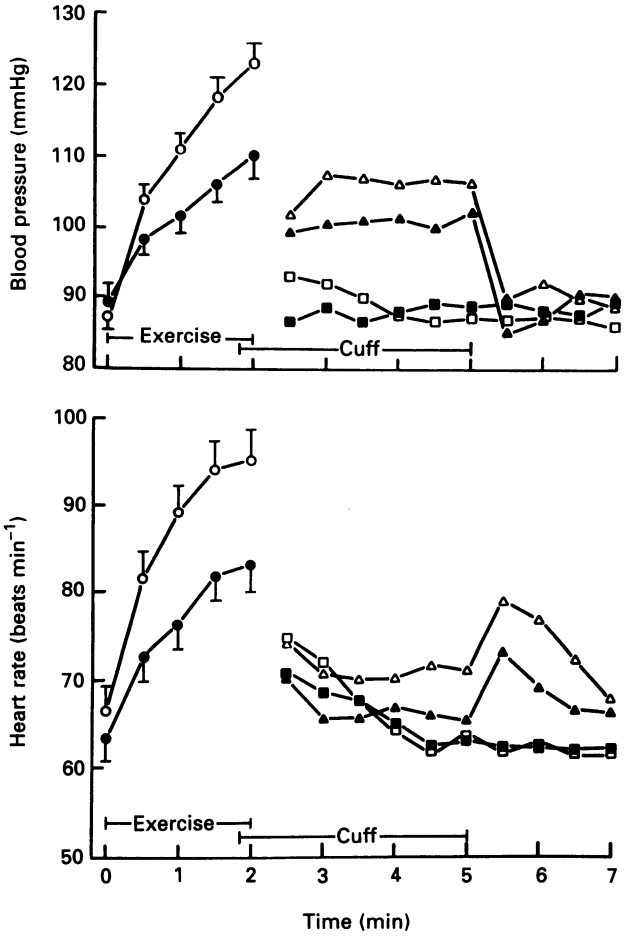

Fig. 2. Average blood pressure and heart rate followed during control contraction and during contractions performed after epidural anaesthesia. Same relative force (30% of the maximal voluntary contraction immediately prior to static exercise). ○, control contraction; ●, contraction during epidural anaesthesia. Values shown from experiments with and without an arterial cuff applied during the last 10 s of the contraction and for the following 3 min of rest. △, control contraction with cuff; ▲, contraction after epidural anaesthesia with cuff; □, control contraction without cuff; ■, contraction after epidural anaesthesia without cuff.

found that position and vibration senses were unimpaired, and, in contrast, light touch and sharp pain senses were slightly diminished, and deep pain and temperature senses were markedly impaired.

Same relative force (30% of the maximal voluntary contraction immediately prior to static exercise)

Static exercise (Fig. 2)

Before static contractions, mean arterial pressure was 88 ± 2 mmHg and heart rate was 65 ± 3 beats min^{-1}. Mean arterial pressure and heart rate values at rest did not differ significantly between control and epidural anaesthesia. During static

contractions, the epidural anaesthesia *vs.* time interaction for mean arterial pressure revealed that control values were greater than values during epidural anaesthesia at 1 min (111 ± 2 *vs.* 102 ± 2 mmHg) and 2 min (123 ± 3 *vs.* 110 ± 3 mmHg) ($P < 0{\cdot}0001$). Similarly, the epidural anaesthesia *vs.* time interaction for heart rate showed

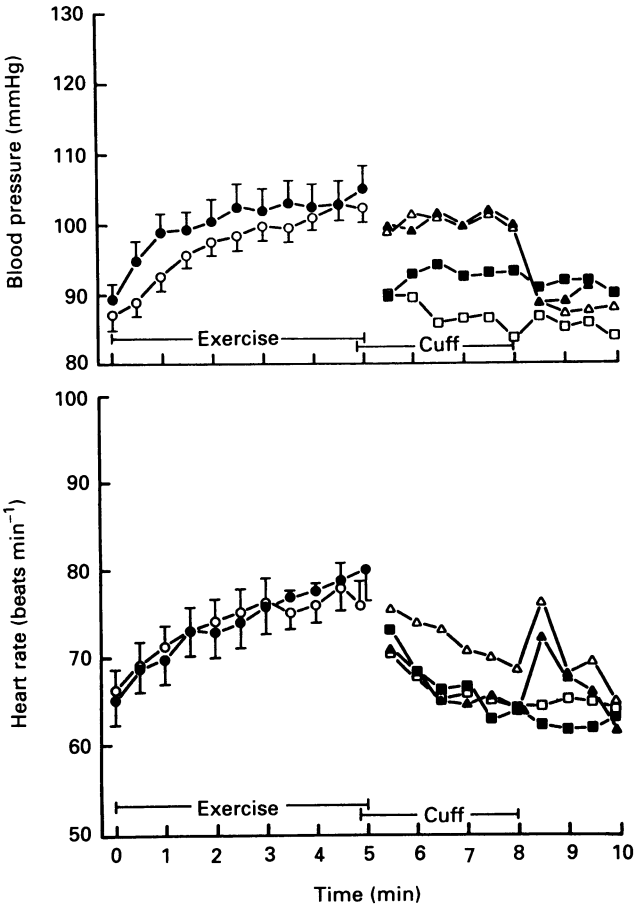

Fig. 3. Average blood pressure and heart rate followed during control contractions and during contractions performed after epidural anaesthesia. Same absolute force (10% of the initial maximal voluntary contraction). ○, control contraction; ●, contraction during epidural anaesthesia. Values shown from experiments with and without an arterial cuff applied during the last 10 s of the contraction and for the following 3 min of rest; △, control contraction with cuff; ▲, contraction during epidural anaesthesia with cuff; □, control contraction without cuff; ■, contraction after epidural anaesthesia without cuff.

control values significantly greater than values during epidural anaesthesia at times 30 s (82 ± 3 *vs.* 73 ± 3 beats min^{-1}), 1 min (89 ± 3 *vs.* 76 ± 3 beats min^{-1}) and 2 min (95 ± 3 *vs.* 83 ± 3 beats min^{-1}) ($P < 0{\cdot}042$). Cuff inflation did not influence the mean arterial pressure or heart rate responses during contraction. The control rating of perceived exertion was not different from the rate of perceived exertion during epidural anaesthesia and the mean value was 16 ± 1 units. Respiratory rate during

static contractions (21 ± 2 breaths min^{-1}) was higher than respiratory rate at rest (17 ± 1 breaths min^{-1}), but no difference existed between values during control and during epidural anaesthesia.

Recovery (Fig. 2)

Mean arterial pressure fell immediately after exercise and reached baseline by the end of recovery. However, arterial cuff occlusion did maintain mean arterial pressure at a higher level than the 'no cuff' treatment at all time levels of recovery ($P < 0{\cdot}0001$). Within the 'cuff' group, six subjects had higher control values than during epidural anaesthesia; none the less, the effect was not significant. Heart rate also fell immediately after exercise and returned to baseline by the end of recovery. A 'cuff' *vs.* time interaction showed heart rate during cuff application was higher than the 'no cuff' treatment at 4·5 min (69 ± 3 *vs.* 62 ± 3 beats min^{-1}) and 5 min (68 ± 3 *vs.* 63 ± 3 beats min^{-1}) ($P < 0{\cdot}0023$). A transient rise in heart rate occurred immediately after cuff deflation for both control and epidural treatments which was probably due to baroreceptor reflex activation. With epidural anaesthesia groups combined across 'cuff' treatments, the respiratory rate during recovery was 1 ± 0 breaths min^{-1} higher without than with the cuff (18 ± 1 *vs.* 19 ± 1 breaths min^{-1}). No difference in respiratory rate existed between control and epidural anaesthesia with cuff occlusion.

Same absolute force (10 % of the initial maximal voluntary contraction)

Static exercise (Fig. 3)

Before static contraction, mean arterial pressure and heart rate were 88 ± 2 mmHg and 66 ± 3 beats min^{-1}, respectively. Values during control and during epidural anaesthesia were similar. Also, during static contractions, the values of mean arterial pressure and heart rate failed to differ during control and during epidural anaesthesia. During exercise both rose steadily to final values of 104 ± 3 mmHg and 78 ± 4 beats min^{-1}, respectively. Cuff inflation had no influence upon the final mean arterial pressure and heart rate values during contraction. The rate of perceived exertion during epidural anaesthesia was 2 ± 1 units higher than during the control study (13 ± 1 *vs.* 11 ± 1 units). Exercise respiratory rate (21 ± 1 breaths min^{-1}) was higher than rest respiratory rate (17 ± 1 breaths min^{-1}) and was unaffected by epidural anaesthesia.

Recovery (Fig. 3)

The cuff maintained mean arterial pressure near exercise level at an average of 101 ± 4 mmHg over its period of application, higher than the 'no cuff' treatment. Epidural anaesthesia did not influence the 'cuff' response. For the control study, mean arterial pressure was higher in the 'cuff' treatment than in the 'no cuff' treatment at 6·5 min (101 ± 4 *vs.* 86 ± 2 mmHg), 7 min (100 ± 3 *vs.* 87 ± 2 mmHg), and 8 min (100 ± 4 *vs.* 84 ± 2 mmHg). Similarly, for epidural anaesthesia, the 'cuff' treatment was higher than the 'no cuff' treatment at 5·5 min (100 ± 4 *vs.* 90 ± 4 mmHg). At 6·5 min and 8 min, the mean arterial pressure for the epidural 'no cuff' treatment was higher than the control 'no cuff' treatment (94 ± 3 *vs.* 84 ± 2 mmHg and 93 ± 3 *vs.* 86 ± 2 mmHg, respectively). Heart rate fell immediately after exercise and time had the only effect upon it during recovery ($P < 0{\cdot}0001$) with all time levels

different from one another. A transient rise in heart rate, in both epidural and control groups, occurred when the cuff was deflated indicating baroreceptor reflex activation. Arterial 'cuff' and 'no cuff' groups did not differ in respiratory rates (18 ± 1 breaths min^{-1}), and neither did control and epidural anaesthesia groups within the 'cuff' treatment.

DISCUSSION

When the same absolute force (10% of the initial maximal voluntary contraction) was maintained, the increases in mean arterial pressure and heart rate were similar during the control study and during epidural anaesthesia. On the other hand, when the same relative force (30% of the maximal voluntary contraction immediately prior to static exercise) was maintained, the increases in mean arterial pressure and heart rate were less during epidural anaesthesia than during the control study. Thus, the findings of this study suggest that the afferent feedback from the working muscle is of importance in determining the cardiovascular response to static exercise. That is, the signal from central command does not determine the magnitude of the increase in blood pressure and heart rate during static exercise when there is lack of feedback from the working muscle.

Respiratory rate during static exercise was unaltered during epidural anaesthesia, similar to the finding that ventilation ($l\ min^{-1}$) during dynamic exercise is also unchanged during epidural anaesthesia (Hornbein *et al.* 1969; Kjær *et al.* 1988). Consistent with the idea that central command during epidural anaesthesia was identical to control during the same relative work, but higher than control during the same absolute work, the rating of perceived exertion did not differ from control in the former, but was higher than control in the latter.

These results are probably not due to blockade of efferent sympathetic nerve fibres to the leg since the resting mean arterial pressure and the response to the cold pressor test and to a Valsalva manoeuvre during epidural anaesthesia were no different than during the control study (Kjær *et al.* 1988). In the present study, a reflex increase in heart rate was seen after cuff deflation and decrease in mean arterial blood pressure in epidural as well as control experiments. Furthermore, noradrenaline levels measured during maximal dynamic exercise are not reduced during epidural anaesthesia (Kjær *et al.* 1988).

The present study confirmed that an arterial occlusion cuff does not fully maintain the mean blood pressure response after static exercise (Leonard *et al.* 1985) as it does after dynamic exercise (Alam & Smirk, 1937; Freund *et al.* 1979; Kjær *et al.* 1988). While the arterial occlusion cuff did maintain mean arterial pressure at a slightly higher level than the 'no cuff' treatment, epidural anaesthesia failed to significantly reduce this response as it does during dynamic exercise (Freund *et al.* 1979; Kjær *et al.* 1988). Given the low level at which the arterial cuff maintains blood pressure after static exercise, it may not be surprising that the epidural anaesthesia failed to significantly effect an additional diminution. Moreover, in the present study, for both the same absolute and relative contractions, as well as after dynamic exercise (Kjær *et al.* 1988), the epidural anaesthesia during circulatory occlusion never entirely abolished the post-exercise blood pressure response, but maintained mean arterial pressure around 100 mmHg, about 10 mmHg above the resting value. This suggests

that a portion of the sensory component of the pressor reflex remains unaffected by epidural anaesthesia.

Nevertheless, other findings suggest that some degree of sensory block was produced. As mentioned earlier, epidural anaesthesia as performed in this study blocks the post-exercise maintenance of the pressor response in dynamically exercising muscles (Freund *et al.* 1979; Kjær *et al.* 1988). The increase in plasma β-endorphin which is unaffected by an increase in central command during dynamic exercise with partial curarization (Kjær, Secher, Bach & Galbo, 1987), is eliminated by epidural anaesthesia (Kjær *et al.* 1988). The large reduction in voluntary motor strength, a function performed by large, myelinated fibres, indicates a simultaneous blockade of small, unmyelinated sensory fibres (De Jong, 1977). Finally, neurological examination of our subjects revealed a gross impairment of deep pain and temperature perception.

Two neural mechanisms that are responsible for the cardiovascular responses to static exercise in man have been proposed (Mitchell & Schmidt, 1983; Mitchell, 1985). However, in experimental models in which one of the components is increased or decreased, the other may produce a near appropriate cardiovascular response. For example, some studies have emphasized the importance of the central neural component (Freyschuss, 1970; Goodwin, McCloskey & Mitchell, 1972; Schibye, Mitchell, Payne & Saltin, 1981; Secher, 1985; Leonard *et al.* 1985) and others have emphasized the importance of the reflex neural component (Alam & Smirk, 1937; Hultgren & Sjöholm, 1982). Also animal studies have shown that cardiovascular responses similar to those occurring during exercise can be produced by either central or reflex neural mechanisms. Again some studies have emphasized the central component (Eldridge, Millhorn & Waldrop, 1981; Hobbs, 1982; Waldrop, Henderson, Iwamoto & Mitchell, 1986) and others have emphasized the reflex component (Coote, Hilton & Perez-Gonzalez, 1971; McCloskey & Mitchell, 1972; Mitchell, Reardon & McCloskey, 1977; Kaufman, Longhurst, Rybicki, Wallach & Mitchell, 1983).

The findings reported in the present study must be viewed alongside the cardiovascular changes observed during maintained static contractions with partial neuromuscular blockade and no effect on afferent feedback from working muscle (Leonard *et al.* 1985; Victor *et al.* 1989; Mitchell *et al.* 1989). In those studies the mean arterial pressure and heart rate increased in proportion to the central command, i.e. they were higher during neuromuscular blockade when the same absolute force (10% of the initial maximal voluntary contraction) was maintained and even continued to increase when force decreased. Further, in the study of Leonard *et al.* (1985), the cardiovascular responses were the same during neuromuscular blockade and the control study when the same relative force (30% of the maximal voluntary contraction immediately prior to static exercise) was maintained and less force was developed. The findings of those studies suggest that central command is of importance in determining the cardiovascular response to static exercise.

However, no discrepancy necessarily exists between the study by Leonard *et al.* (1985) and the present findings. Rather the present study using epidural anaesthesia, which produced partial motoneurone blockade (muscle weakness) accompanied by some degree of sensory blockade, allows additional conclusions to those made from

the study by Leonard *et al.* (1985) and this is shown in Fig. 4. In subjects during a control study, both the central and reflex neural mechanisms act in concert to produce the cardiovascular responses at 10% and at 30% of the maximal voluntary contraction. In subjects during epidural anaesthesia, the changes in mean arterial

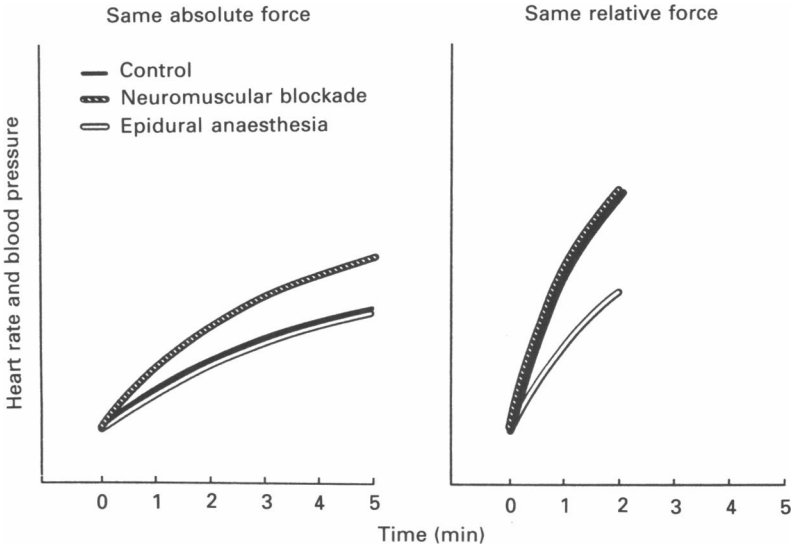

Fig. 4. Summary of the effects of neuromuscular blockade and of epidural anaesthesia on the cardiovascular response to static exercise. The effect of each intervention as compared to the control response is shown at the same absolute force in the left panel and at the same relative force in the right panel. (For description, see text.)

pressure and heart rate were less at the same relative work load than during the control study, but no different at the same absolute work load (Fig. 4). When the same absolute force is maintained during epidural anaesthesia, the effect of increased central command during motoneurone blockade (muscle weakness) is counterbalanced by a decrease in afferent feedback from the contracting muscle and the cardiovascular response is the same as during the control study (Fig. 4). Likewise when the same relative force is maintained during epidural anaesthesia, the effect of the same central command is diminished by a decrease in afferent feedback from the contracting muscle and the cardiovascular response is less during epidural anaesthesia. On the other hand, in subjects during neuromuscular blockade when the same absolute force is maintained, the effect of increased central command is not counterbalanced by a change in afferent feedback from the contracting muscle and the cardiovascular response is greater during neuromuscular blockade than during the control study (Fig. 4). Also, when the same relative force is maintained during neuromuscular blockade, the effect of the same central command is not diminished by a decrease in afferent feedback from the contracting muscle and the cardiovascular response is the same.

The results from the present study and those from the study by Leonard *et al.* (1985) are complimentary and suggest that both central and reflex neural mechanisms play important roles in regulating arterial blood pressure and heart rate

during static exercise in man. Even though their manner of neural integration remains unknown, the two mechanisms appear to be somewhat redundant, rather than simply additive, and to impinge on the same regulatory nerve cells in the cardiovascular control areas where neural occlusion is operative.

This work was supported by the Danish Medical Research Council, the Frank M. Ryburn Jr Chair in Heart Research, La Cour's Fund, and the Lawson and Rogers Lacy Research Fund in Cardiovascular Diseases. We thank Professor A. Guz for conducting a neurological examination on two of the subjects, and Ms Jan Wright for her excellent help in preparing the manuscript.

REFERENCES

ALAM, M. & SMIRK, F. M. (1937). Observations in man upon a blood pressure raising reflex arising from the voluntary muscles. *Journal of Physiology* **89**, 372–383.

ALAM, M. & SMIRK, F. M. (1938). Observations in man on a pulse-accelerating reflex from the voluntary muscles of the legs. *Journal of Physiology* **92**, 167–177.

BORG, G. (1970). Perceived exertion as an indicator of somatic stress. *Scandinavian Journal of Rehabilitation Medicine* **2–3**, 92–98.

COOTE, J. H., HILTON, S. M. & PEREZ-GONZALEZ, J. F. (1971). The reflex nature of the pressor response to muscular exercise. *Journal of Physiology* **215**, 789–804.

DE JONG, R. H. (1977). *Local Anesthetics*, pp. 51–83. Springfield, Il, USA: Thomas.

ELDRIDGE, F. L., MILLHORN, D. E. & WALDROP, T. G. (1981). Exercise hyperpnea and locomotion: Parallel activation from the hypothalamus. *Science* **211**, 844–846.

FREUND, P. R., ROWELL, L. B., MURPHY, T. M., HOBBS, S. F. & BUTLER, S. H. (1979). Blockade of the pressor response to muscle ischemia by sensory nerve block in man. *American Journal of Physiology* **236**, H433–439.

FREYSCHUSS, U. (1970). Cardiovascular adjustment to somatomotor activation. *Acta physiologica scandinavica* **342**, suppl., 1–63.

GOODWIN, G. M., MCCLOSKEY, D. I. & MITCHELL, J. H. (1972). Cardiovascular and respiratory responses to changes in central command during isometric exercise at constant muscle tension. *Journal of Physiology* **226**, 173–190.

HOBBS, S. F. (1982). Central command during exercise: parallel activation of the cardiovascular and motor systems by descending command signals. In *Circulation, Neurobiology and Behavior*, ed. SMITH, O. A., GALOSY, R. A. & WEISS, S. M., pp. 217–231. New York: Elsevier Biomedical.

HORNBEIN, T. F., SØRENSEN, S. C. & PARKS, C. R. (1969). Role of muscle spindles in lower extremities in breathing during bicycle exercise. *Journal of Applied Physiology* **27**, 476–479.

HULTMAN, E. & SJÖHOLM, H. (1982). Blood pressure and heart rate response to voluntary and non-voluntary static exercise in man. *Acta physiologica scandinavica* **115**, 499–501.

KAUFMAN, M. P., LONGHURST, J. C., RYBICKI, K. J., WALLACH, J. H. & MITCHELL, J. H. (1983). Effects of static muscular contraction on impulse activity of groups III and IV afferents in cats. *Journal of Applied Physiology* **55**, 105–112.

KJÆR, M., SECHER, N. H., BACH, G. W. & GALBO, H. (1987). Role of motor center activity for hormonal changes and substrate mobilization in exercising man. *American Journal of Physiology* **253**, R687–695.

KJÆR, M., SECHER, N. H., FERNANDES, A., GALBO, H., THOMAS, S. & MITCHELL, J. H. (1988). Cardiovascular and respiratory responses to dynamic exercise in man with sensory, nervous blockade (abstract). *Medicine and Science in Sports and Exercise* **20**, suppl., 82.

LASSEN, A., MITCHELL, J. H., REEVES, JR, D. R., ROGERS, H. B. & SECHER, N. H. (1989). Cardiovascular responses to brief static contractions in man with topical nervous blockade. *Journal of Physiology* **409**, 333–341.

LEONARD, B., MITCHELL, J. H., MIZUNO, M., RUBE, N., SALTIN, B. & SECHER, N. H. (1985). Partial neuromuscular blockade and cardiovascular responses to static exercise in man. *Journal of Physiology* **359**, 365–379.

MCCLOSKEY, D. I. & MITCHELL, J. H. (1972). Reflex cardiovascular and respiratory responses originating in exercising muscle. *Journal of Physiology* **224**, 173–186.

MITCHELL, J. H. (1985). Cardiovascular control during exercise: Central and reflex neural mechanisms. *American Journal of Cardiology* **55**, 34–41D.

MITCHELL, J. H., KAUFMAN, M. P. & IWAMOTO, G. A. (1983). The exercise pressor reflex: Its cardiovascular effects, afferent mechanisms, and central pathways. *Annual Review of Physiology* **45**, 229–242.

MITCHELL, J. H., REARDON, W. C. & MCCLOSKEY, D. I. (1977). Reflex effects on circulation and respiration from contracting skeletal muscle. *American Journal of Physiology* **233**, H374–378.

MITCHELL, J. H., REEVES JR, D. R., ROGERS, H. B., SECHER, N. H. & VICTOR, R. G. (1989). Autonomic blockade and cardiovascular responses to static exercise in partially curarized man. *Journal of Physiology* **413**, 433–445.

MITCHELL, J. H. & SCHMIDT, R. F. (1983). Cardiovascular reflex control by afferent fibers from skeletal muscle receptors. In *Handbook of Physiology*, ed. SHEPHERD, J. T. & ABBOUD, F. M. pp. 623–658. Bethesda, MD, USA: American Physiological Society.

SCHIBYE, B., MITCHELL, J. H., PAYNE III, F. C. & SALTIN, B. (1981). Blood pressure and heart rate response to static exercise in relation to electromyographic activity and force development. *Acta physiologica scandinavica* **113**, 61–66.

SECHER, N. H. (1985). Heart rate at the onset of static exercise in man with partial neuromuscular blockade. *Journal of Physiology* **368**, 481–490.

VICTOR, R. G., PRYOR, S. L., MITCHELL, J. H. & SECHER, N. H. (1989). Effects of partial neuromuscular blockade on sympathetic nerve responses to static exercise in humans. *Circulation Research* **65** (2).

WALDROP, T. G., HENDERSON, M. C., IWAMOTO, G. A. & MITCHELL, J. H. (1986). Regional blood flow responses to stimulation of the subthalamic locomotor region. *Respiration Physiology* **64**, 93–102.