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AUTONOMIC BLOCKADE AND CARDIOVASCULAR RESPONSES TO STATIC EXERCISE IN PARTIALLY CURARIZED MAN

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SUMMARY

1. The cardiovascular responses, heart rate and mean arterial pressure, were followed in seventeen human subjects who performed static handgrip contractions for 2 min at the same absolute force (15% of the initial maximal voluntary contraction strength) before and during partial curarization. In control contractions the rate of perceived exertion was 10 exertion units, 16 units in contractions with tubocurarine which could be maintained and 20 units in contractions that could not be maintained. Control contractions increased mean arterial pressure by 6 mmHg from 89 mmHg while heart rate was unchanged from the resting value of 68 beats min^{-1}. With tubocurarine, larger increases in mean arterial pressure of 11 mmHg and for heart rate of 8 beats min^{-1} were obtained during maintained contractions, and 15 mmHg and 16 beats min^{-1}, respectively, during non-maintained contractions.

2. Atropine increased resting heart rate and blood pressure with tubocurarine to 107 beats min^{-1} and 98 mmHg, respectively, in seven subjects. The blood pressure response to exercise with tubocurarine was unaffected by atropine, but the heart rate increase was reduced from 15 to 4 beats min^{-1}.

3. Propranolol reduced resting heart rate with tubocurarine to 56 beats min^{-1} with no effect on blood pressure in seven subjects. The cardiovascular responses to exercise with tubocurarine were unaffected by propranolol. In contrast, phentolamine reduced resting blood pressure with tubocurarine to 80 mmHg without affecting heart rate in seven subjects. Exercise responses with tubocurarine were unaffected by phentolamine. Combinations of atropine and propranolol in fourteen subjects or atropine and phentolamine in five subjects showed similar results during exercise with tubocurarine as with the sole use of the agents used to block autonomic receptors.

4. The results suggest that when partial curarization induces a disproportion between the signal from central command and that from exercising muscles, the larger signal arising from central command determines the magnitude of the cardiovascular responses. The centrally generated heart rate response is in part caused by vagal withdrawal. However, the blood pressure response cannot be

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attenuated by the sole use of α- or β-receptor adrenergic blockade or combinations of these with atropine. This suggests that there may be greater redundancy in the autonomic control of blood pressure than in the vagal control of heart rate associated with central command during static exercise in man.

INTRODUCTION

Factors in the central nervous system ('central command') as well as reflexes originating in the working muscles are of importance for the increases in heart rate and mean arterial pressure during exercise (Mitchell, Kaufman & Iwamoto, 1983; Mitchell & Schmidt, 1983; Mitchell, 1985). The use of partial neuromuscular blocking agents during voluntary exercise makes it possible to induce a disproportion between an increase in central command and a constant or decreasing signal from receptors responding to muscle tension and metabolism. Using this model it has been demonstrated that heart rate and blood pressure become lower when work intensity decreases during dynamic leg exercise with partial curarization (Galbo, Kjaer & Secher, 1987). In contrast an increase in heart rate and blood pressure has been demonstrated during static exercise when force cannot be maintained due to partial neuromuscular blockade (McCloskey, 1981; Hobbs, 1982; Leonard, Mitchell, Mizuno, Rube, Saltin & Secher, 1985) possibly reflecting a centrally mediated decrease in parasympathetic and increase in sympathetic nervous activity (Pryor, Mitchell, Secher & Victor, 1987).

In the present study two doses of tubocurarine were used in order to evaluate whether the heart rate and blood pressure responses to a static handgrip in partially curarized man increase in proportion to the involved central command, i.e. whether they increase more if the subject is unable to maintain the contraction than when the contraction can be maintained. The mechanisms involved in increasing heart rate and blood pressure during exercise with partial curarization were evaluated by blocking the parasympathetic nervous system with atropine, the sympathetic α-adrenergic receptors with phentolamine and the β-adrenergic receptors with propranolol. In addition combinations of atropine and the two adrenergic blocking agents were used.

METHODS

Seventeen healthy subjects (five females and twelve males) were studied. Their mean age was 28 years (range, 21–46 years), weight 75 kg (range, 57–110 kg) and height 179 cm (range, 160–192 cm). None of the subjects was taking any medication and all were informed of the inconveniences involved with the participation in the experiment before giving their oral consent. Furthermore, most of the subjects had previously participated in similar experiments. The study was approved by the Municipal Ethical Committee of Copenhagen.

Experiments were performed with the subjects lying in a semisupine position on a couch. During experiments with phentolamine the lower legs were placed on a shelf at heart level. Each experiment involving a sustained handgrip contraction of 2 min duration was preceded by a 2 min rest period and followed by 2 min of recovery. In all contractions a force corresponding to 15% of the subjects' initial maximal voluntary contraction strength was attempted. Each setting (tubocurarine and tubocurarine with atropine, phentolamine or propranolol, or tubocurarine with combinations of atropine and phentolamine or atropine and propranolol) was carried out twice. In the first contraction a dose of tubocurarine was used to reduce strength to approximately 40% of control in order to make the subject unable to maintain force corresponding to 15% of the subjects'

initial voluntary contraction strength throughout the 2 min contraction. In the second contraction, a 50% reduction in strength was aimed at in order to enable the subject to maintain force. If this goal was not obtained, i.e. if the subject was able to maintain the contraction when aiming at a 'non-maintained' contraction, or vice versa, the experiment was repeated until the target was obtained. After each experiment the subject was asked to rate his perceived exertion on a scale from 6 to 20 (Borg, 1970). On this scale 6 exertion units represents very, very light and 20 very very hard exertion. If the perceived exertion was rated lower than '20' during a non-maintained contraction, the subject was asked in addition to indicate how hard he tried, using the same scale. Whenever a record of respiration showed that the subject held his breath during the contraction or that electromyographic activity was detectable in the leg, the experiment was not accepted. Another experiment was conducted under normal breathing even when the effort was maximal, and the subject was asked not to tighten muscle groups other than those directly involved in the handgrip contraction.

Experiments involving atropine, propranolol and phentolamine (seven subjects each) were conducted in separate weeks. In the first week experiments involved (a) a control contraction, (b) contractions with tubocurarine, (c) contractions with tubocurarine and propranolol and (d) contractions with tubocurarine, propranolol and atropine. In the following week control experiments (a) were followed by contractions with tubocurarine (b), with tubocucarine and atropine (c), and with tubocurarine, atropine and propranolol (d). In the third week contractions were performed as control (a), with tubocurarine (b), with tubocurarine and phentolamine (c) and with tubocurarine, phentolamine and atropine (d). Experiments using tubocurarine, atropine and propranolol thus involved fourteen subjects. Two subjects did not want to repeat the experience involved in the use of atropine so the experiment involving atropine, phentolamine and tubocurarine was conducted with only five subjects. Resting periods between contractions were allowed for administration of drugs and titrating the approximate level of partial curarization.

Bipolar electrocardiographic electrodes were applied to the chest and heart rate was integrated over 6 s on a Simonsen & Weel electrocardiogram trendscope. A 1 mm arterial cannula was placed in the brachial artery of the non-dominant arm and connected to a Bentley transducer (800) positioned at heart level in the mid-axillary line and mean arterial pressure was electrically integrated over 6 s on the Simonsen & Weel monitoring apparatus (8041). The cannula was kept patent by constant flush of 3 ml saline h^{-1}. Respiratory excursions were recorded using a strain-gauge pneumograph. Electromyographic activity on the right thigh was recorded by means of a DISA electromyogram amplifier ISOI and a built-in mean voltage unit. Handgrip strength of the dominant arm was measured with strain-gauge apparatus (Asmussen, Heebøll-Nielsen & Molbech, 1959) and a Peekel measuring bridge. All variables were recorded on an Elema writer. Arterial blood samples were analysed on a Radiometer ABL-4 machine for pH, oxygen and carbon dioxide tensions.

A venous line on the non-dominant hand was used to administer tubocurarine (Nordisk Droge), propranolol (Frekven, Ferrosan), atropine (DAK) and phentolamine (Regitina, Ciba). All drugs were administered under constant flush of saline for approximately 1 min. Tubocurarine was given as a bolus of 0·1 mg kg^{-1} with small supplementary doses in order to achieve the aimed reduction in strength before each contraction. Atropine was given slowly to a total dose of 0·06 mg kg^{-1}. A supplementary dose of 0·5 mg of atropine was added before following experiments with atropine. The dose of propranolol was 0·15 mg kg^{-1} which was given slowly over approximately 5 min, and the experiments began 5 min after the last administration. Phentolamine was given as a fixed dose of 5 mg. Heart rate and blood pressure were constantly monitored during drug administration. An ambu-E resuscitator apparatus and neostigmine were at all times available, but were never needed.

Data were calculated as the means of all accepted experiments performed during one circumstance in a given subject. Four subjects participating in two experiments. The median values of these averages are presented with the range (in parentheses) for each circumstance involving from five to seventeen subjects. In experiments involving autonomic blockade values are presented as averages of the non-maintained and maintained contraction series. Resting values were expressed as the average of four recorded determinations. Friedman's test was used to test if significant changes occurred with time (Siegel, 1956). Wilcoxon's ranking test for unpaired and paired data (Pratt's modification) was used to evaluate differences between circumstances. Where five subjects were investigated Student's paired t test was applied. A P value of 0·05 was considered significant.

RESULTS

Control contractions (n = 17)

At rest arterial oxygen and carbon dioxide tensions were 12·1 (9·2–15·8) and 5·1 (4·1–5·2) kPa, respectively, and pH was 7·39 (7·39–7·44) in the seventeen subjects. Control strength was 579 (294–638) N.

During contractions at 15% of the subjects' initial voluntary contraction strength in which there was no increase in electromyographic activity on the right thigh and

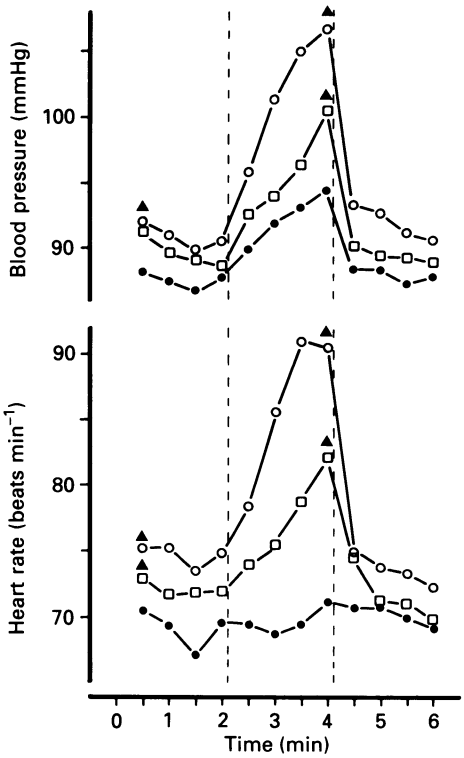

Fig. 1. Mean values ($n = 17$) for mean arterial blood pressure and heart rate followed at rest, during a 2 min sustained handgrip contraction corresponding to 15% of the initial maximal contraction strength and for the following 2 min of recovery. ●, control contraction; □, contraction with tubocurarine which the subjects were able to maintain; ○, contraction with tubocurarine which the subjects were unable to maintain throughout the 2 min contraction. ▲, resting values and exercise responses obtained with tubocurarine are different ($P < 0·05$) from control. Dashed lines demarcate the 2 min contraction period.

that subject did not hold his breath, mean blood pressure was 89 (67–104) mmHg and increased to 95 (76–106) mmHg at the end of the 2 min sustained contraction ($P < 0·01$; Fig. 1). The control contractions did not increase heart rate significantly from the resting value of 68 (53–100) beats min^{-1} (Fig. 1). After termination of the contraction blood pressure returned to the resting values. The rating for perceived exertion was 10 (6–13) units.

Partial curarization

Maintained contractions (n = 17)

Handgrip strength was reduced to 55 (44–90) % of control strength by the administration of tubocurarine. Blood pressure at rest was 91 (71–101) mmHg, and was not significantly different from control at 15 % of the subjects' initial voluntary contraction strength. During the contraction it increased to 101 (86–113) mmHg

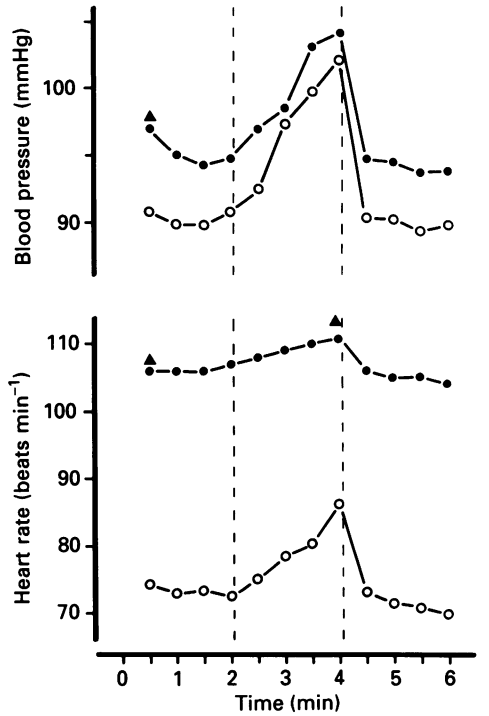

Fig. 2. Mean values ($n = 7$) for mean blood pressure and heart rate during a 2 min sustained contraction corresponding to 15 % of the initial maximal contraction strength. Values are averages of maintained and non-maintained contractions. ○, tubocurarine; ●, atropine and tubocurarine. ▲, resting values and exercise responses obtained with atropine and tubocurarine are different ($P < 0{\cdot}02$) from those obtained with tubocurarine only.

($P < 0{\cdot}01$) which was between the values observed during control and non-maintained contractions ($P < 0{\cdot}05$; Fig. 1). Heart rate at rest was 72 (54–107) beats min^{-1} or higher than during control ($P < 0{\cdot}05$). During exercise a value of 80 (56–123) beats min^{-1} was obtained ($P < 0{\cdot}01$; Fig. 1). The responses to exercise were larger than during control ($P < 0{\cdot}05$), but smaller than during the non-maintained contractions ($P < 0{\cdot}01$). The rating for perceived exertion was 16 (9–18) units.

Non-maintained contractions (n = 17)

Handgrip strength was reduced to 44 (24–70) % of control strength which was significantly more ($P < 0{\cdot}01$) than before the maintained contractions in seventeen

subjects. At rest arterial oxygen and carbon dioxide tensions were 13·2 (9·8–16·2) and 4·9 (4·4–5·3) kPa, respectively, and pH was 7·41 (7·38–7·42), not significantly different from control.

Blood pressure at rest was 92 (72–107) mmHg, i.e. higher than during control ($P < 0·02$). During exercise it increased to 109 (78–122) mmHg ($P < 0·01$; Fig. 1) and returned to the resting value after exercise. Also, heart rate at rest, 75 (56–121) beats

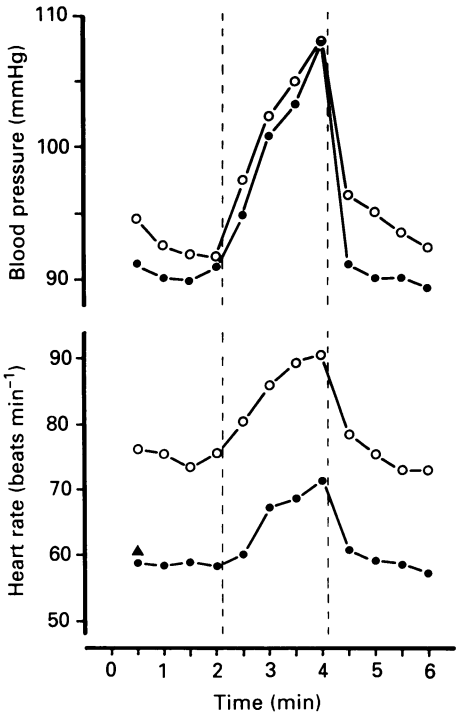

Fig. 3. Mean values ($n = 7$) for mean blood pressure and heart rate during a 2 min sustained contraction corresponding to 15% of the initial maximal contraction strength. Values are averages of maintained and non-maintained contractions. ○, tubocurarine; ●, propranolol and tubocurarine. ▲, heart rate at rest with propranolol and tubocurarine is different ($P < 0·05$) from that obtained with tubocurarine only.

min^{-1}, was higher than during control ($P < 0·01$; Fig. 1). During exercise a further increase to 91 (74–106) beats min^{-1} ($P < 0·01$) was obtained and heart rate decreased to the resting value after the contraction. Both the heart rate and blood pressure responses to exercise were larger than during the control contractions ($P < 0·01$). The rating for perceived exertion was 20 (17–20) units and thus was larger than during the control contractions. In all experiments where the rating for perceived exertion was lower than 20, the subjects indicated that they had tried to sustain the contraction corresponding to an intensity rated as '20'.

Partial curarization and atropine ($n = 7$)

The averaged maintained and non-maintained contraction strength was reduced to 47 (23–68)% of control and was similar to that obtained with tubocurarine alone. Blood pressure at rest was 98 (75–111) mmHg which was higher ($P < 0·02$) than with

tubocurarine alone (95 (71–100) mmHg) (Fig. 2) in the seven subjects. During the contraction the increase in blood pressure with and without atropine were similar. Heart rate at rest was 107 (92–115) beats min^{-1} with atropine which was also higher ($P < 0{\cdot}02$) than with tubocurarine alone (75 (57–84) beats min^{-1}). With atropine the

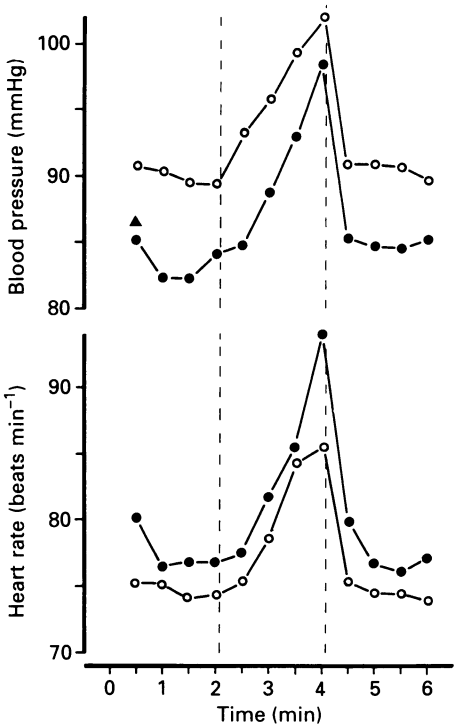

Fig. 4. Mean values ($n = 7$) for mean blood pressure and heart rate during a 2 min sustained contraction corresponding to 15% of the initial maximal contraction strength. Values are averages of maintained and non-maintained contractions. ○, tubocurarine; ●, phentolamine and tubocurarine; ▲, resting blood pressure with phentolamine and tubocurarine is different ($P < 0{\cdot}02$) from that obtained with tubocurarine only.

contraction-induced increase was reduced from 15 (3–22) beats min^{-1} with tubocurarine alone to 4 (−4–6) beats min^{-1} ($P < 0{\cdot}02$; Fig. 2) and was not significantly different from zero. The rating for perceived exertion was 18 (17–19) units with atropine, similar to that expressed with tubocurarine alone.

Partial curarization and propranolol ($n = 7$)

The averaged maintained and non-maintained contractions strength was reduced to 44 (32–64)% of control and was similar to the reduction in strength after tubocurarine. Blood pressure at rest and during the contraction with tubocurarine was unaffected by propranolol (Fig. 3) in the seven subjects. Heart rate at rest was reduced by propranolol to 56 (52–69) beats min^{-1} ($P < 0{\cdot}05$), but the exercise response was similar to that obtained with tubocurarine alone (Fig. 3). The rating of perceived exertion was 19 (17–20) units, similar to that expressed after the contraction with tubocurarine alone.

Partial curarization and phentolamine ($n = 7$)

The averaged maintained and non-maintained contraction strength was reduced to 60 (49–72)% and was similar to that seen with tubocurarine only. Phentolamine reduced blood pressure at rest from 87 (78–103) to 80 (74–97) mmHg ($P < 0{\cdot}02$), but did not change the exercise response (Fig. 4) in the seven subjects. Heart rate at rest and during the contraction was not affected significantly by phentolamine (Fig. 4).

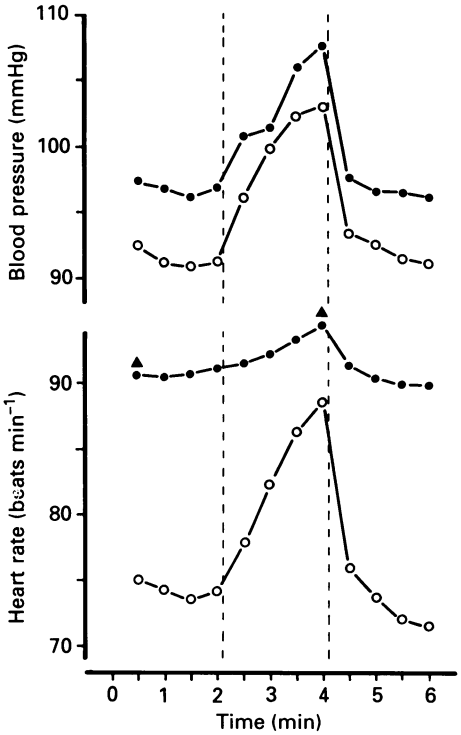

Fig. 5. Mean values ($n = 14$) for mean blood pressure and heart rate during a 2 min sustained contraction corresponding to 15% of the initial maximal contraction strength. Values are averages of maintained and non-maintained contractions. ○, tubocurarine; ●, atropine, propranolol and tubocurarine. ▲, heart rate at rest and the exercise response with atropine, propranolol and tubocurarine are different ($P < 0{\cdot}01$) from those obtained with tubocurarine only.

The rating for perceived exertion was 17 (15–20) units with phentolamine, similar to that expressed with tubocurarine alone.

Partial curarization and atropine with propranolol (n = 14)

The averaged maintained and non-maintained contraction strength was reduced to 52 (20–60)% of control and was similar to that obtained with tubocurarine alone. Resting blood pressure was 93 (71–119) mmHg and was not significantly different from rest with tubocurarine alone. Also the exercise responses were similar (Fig. 5) in the fourteen subjects. In contrast heart rate at rest was higher (94 (77–119) beats min^{-1}) than with tubocurarine alone, (74 (57–114) beats min^{-1}; $P < 0{\cdot}01$; Fig. 5),

although not as large as with atropine and tubocurarine (107 (92–115) beats min^{-1}; $P < 0{\cdot}02$; Fig. 2). The exercise increase was reduced from 11 (4–36) to 2 (0–19) beats min^{-1} ($P < 0{\cdot}01$) and was not significantly different from that obtained with tubocurarine and atropine, but was higher than zero ($P < 0{\cdot}01$). The rating for perceived exertion was 19 (17–20) units with atropine and propranolol and was not significantly different from that given for exercise with tubocurarine only.

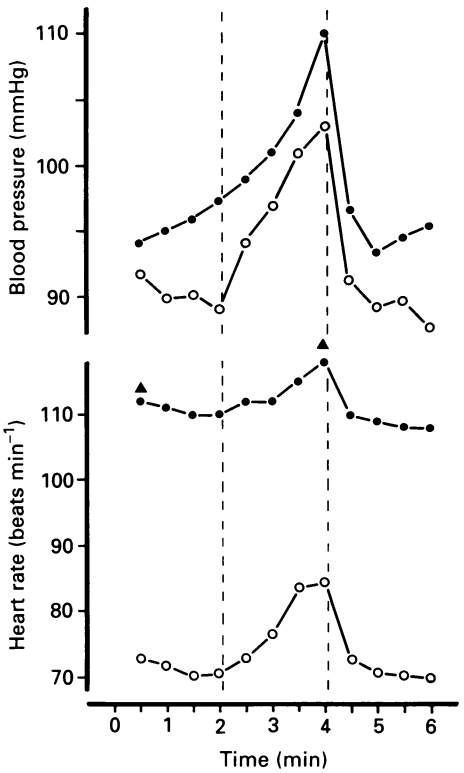

Fig. 6. Mean values ($n = 5$) for mean blood pressure and heart rate during a 2 min sustained contraction corresponding to 15% of the initial maximal contraction strength. Values are averages of maintained and non-maintained contractions. ○, tubocurarine; ●, atropine, phentolamine and tubocurarine. ▲, heart rate at rest and the exercise response with atropine, phentolamine and tubocurarine are different ($P < 0{\cdot}01$) from that obtained with tubocurarine only.

Partial curarization and atropine with phentolamine ($n = 5$)

The averaged maintained and non-maintained contraction strength was reduced to 56 (41–61) % of control and was similar to that obtained with tubocurarine alone. Blood pressure at rest was 95 (81–120) mmHg and similar to that obtained with tubocurarine alone (Fig. 6) in the five subjects. Also the exercise-induced increase in blood pressure was similar in the two experimental situations. In contrast heart rate was higher with atropine and phentolamine: 106 (100–138) *vs.* 73 (54–79) beats min^{-1} ($P < 0{\cdot}01$; Fig. 6). During the contraction the heart rate response was reduced from 12 (9–24) to 4 (0–19) beats min^{-1} ($P < 0{\cdot}01$) and was similar to the response seen with

tubocurarine and atropine, i.e. not significant. The rating for perceived exertion was 19 (18–20) units with atropine and phentolamine, similar to that given with tubocurarine only.

DISCUSSION

Several previous studies have examined effects of autonomic blocking drugs on cardiovascular responses to static exercise in humans. In the present study the effects of autonomic blockade on the cardiovascular responses to handgrip contractions during partial curarization were examined. Since partial neuromuscular blockade should augment the influence of central command without affecting the influence of reflexes arising in exercising muscles or baroreceptors, the findings in this model may provide insight into the efferent autonomic pathways that mediate effects of central command on arterial pressure and heart rate.

In this study the heart rate and blood pressure responses to static exercise with partial curarization were larger than during the control contractions, and the responses were larger when the subjects were unable to maintain force than when force could be maintained after tubocurarine. Previously we have provided evidence for such a relationship between the cardiovascular responses to static exercise with leg contractions and the central command involved (Leonard *et al.* 1985). The quality of the present data are, however, improved by registration of respiratory excursions and electromyographic activity over a resting muscle group (the thigh). A Valsalva-like manoeuvre and the involvement of muscles other than those of primary importance for the handgrip contraction were thus minimized. Furthermore, in the study of Leonard *et al.* (1985) the maintained contractions were performed with decamethonium while the non-maintained contractions were performed with tubocurarine. This means that the larger exercise response seen with tubocurarine could have been due to a relatively selective block of slow and fast twitch muscle fibres with tubocurarine and decamethonium, respectively (Paton & Zaimis, 1951; Secher, Rube & Secher, 1982). It has been suggested that the cardiovascular responses to static exercise are dependent on the involvement of fast twitch muscle fibres (Juhlin-Dannfelt, Frisk-Holmberg, Karlsson & Tesch, 1979; Fallentin, Sidenius & Jørgensen, 1985), although slow twitch muscle fibres are also able to elicit the responses (Iwamoto & Botterman, 1985).

The present results were obtained with two levels of partial curarization in order to induce a progressive involvement of central command. The results support our previous conclusion (Leonard *et al.* 1985), i.e. that the higher heart rate and blood pressure responses seen with non-maintained compared to maintained contractions are due to a difference in central command rather than to a possible difference in the involvement of the two major muscle fibre types. From these results we would suggest that the tendency for enhancement of the cardiovascular responses to static exercise involving fast twitch fibres is due to the fact that these fibres have the highest innervation threshold and are the most fatigable (Burke & Edgerton, 1975). Their involvement thereby becomes an indication of the contraction intensity and thus of central command. This conclusion is supported by the finding that higher cardiovascular responses seen with tubocurarine than with control contractions are

tied to the mode of exercise, i.e. they are seen during static (McCloskey, 1981; Hobbs, 1982; Leonard *et al.* 1985) but not during dynamic exercise (Galbo *et al.* 1987).

In comparison with the previous study involving leg muscles during static exercise with neuromuscular blockade (Leonard *et al.* 1985), the present cardiovascular responses were modest. Without neuromuscular blockade it has been demonstrated that the cardiovascular responses to static exercise increases with the involvement of a larger muscle mass (Mitchell, Payne, Saltin & Schibye, 1980; Seals, Washburn, Hansen, Painter & Nagel, 1983). Taken together, the present study and the previous study with leg extension suggest that the central nervous influence on cardiovascular responses is dependent on the muscle mass involved. Furthermore, this 'central' muscle mass effect is present from the onset of static exercise (Secher, 1985).

While the control contractions elicited an increase in blood pressure, there was no significant heart rate response. In fact heart rate tended to decrease at the beginning of the control contractions (Fig. 1). Previously an unchanged heart rate or a decrease has been reported at the onset of submaximal static finger and handgrip contractions involving an intensity of less than 50% of maximal effort (Secher, 1985).

Heart rate at rest was unaffected by the low dose of tubocurarine, but increased with the higher dose (Fig. 1). The increase in heart rate seen after the high dose of tubocurarine was, however, small (7 beats min^{-1}) as compared with the effect of atropine (32 beats min^{-1}). Although we have not previously seen such an effect (Leonard *et al.* 1985; Kjær, Secher, Bach & Galbo, 1987; Pryor *et al.* 1987) an increase in heart rate after tubocurarine is to be expected due to its vagolytic effect (Hughes & Chapple, 1976). The small increase in resting blood pressure after tubocurarine may also be due to vagal block as resting blood pressure increased after atropine (Fig. 2).

In the present study arterial oxygen and carbon dioxide tensions were unaffected by the highest administered dose of tubocurarine, in accordance with our previous experience (Kjær *et al.* 1987). Thus, although the measured handgrip strength values may not accurately reflect the degree of neuromuscular blockade during the contractions because of the recorded 2 min of rest before each contraction, none of the subjects was blocked to a degree where respiration was affected. This is explained by the fact that the diaphragm is spared by tubocurarine (De Troyer, Bastenier & Delhez, 1980).

Atropine substantially attenuated the heart rate response to static exercise with tubocurarine (Fig. 2). It has been demonstrated that the immediate increase in heart rate at the onset of static exercise is eliminated by atropine (Freyschuss, 1970; Hollander & Bouman, 1975). Furthermore, in the study by Martin, Shaver, Leon, Thomson, Reddy & Leonard (1974) the heart rate response to static exercise was also attenuated by atropine. The results of this study suggests that withdrawal of vagal tone to the sinus node by central command is an important mechanism for the heart rate response to static exercise (Pryor *et al.* 1987).

Phentolamine lowered blood pressure and propranolol lowered heart rate at rest but the two drugs were not able to affect the exercise-induced cardiovascular responses during partial curarization. Martin *et al.* (1974) saw that the heart rate response to static exercise was eliminated by the combined use of atropine (2 mg) and propranolol in the same doses as used in the present study. It could be speculated

that central command was more involved during the contraction in our study. It remains, however, to be shown if higher doses of propranolol in combination with atropine could block the response, or if combined α- and β-adrenergic receptor blockade (McAllister, 1979) is needed to eliminate the cardiovascular responses to static exercise involving a maximal effort. Alternatively, non-adrenergic mechanisms may be involved, i.e. release of other presser agents from peripheral sympathetic nerve terminals affecting vascular smooth muscle which are not blocked by phentolamine.

In conclusion, the cardiovascular responses to static exercise are influenced by central nervous mechanisms and increase in proportion to the involved central command independently of the force generated by the muscles. While the larger part of this effect of central command on heart rate is due to vagal withdrawal, the precise autonomic pathways involved in the regulation of blood pressure remain to be determined. Blockade of α- or β-adrenergic receptors alone or in combination with atropine does not affect the blood pressure response during partial curarization. This suggests that there may be greater redundancy in the autonomic control of blood pressure than in the vagal control of heart rate associated with central command.

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REFERENCES

ASMUSSEN, E., HEEBØLL-NIELSEN, K. & MOLBECH, S. (1959). Methods for evaluation of muscle strength. *Communications from the Danish National Association for Infantile Paralysis* **5**.

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

BURKE, E. R. & EDGERTON, V. R. (1975). Motor unit properties and selective involvement in movement. *Exercise and Sport Sciences Reviews* **3**, 31–81.

DE TROYER, A., BASTENIER, J. & DELHEZ, L. (1980). Function of respiratory muscle during partial curarization in humans. *Journal of Applied Physiology* **49**, 1049–1056.

FALLENTIN, N., SIDENIUS, B. & JØRGENSEN, K. (1985). Blood pressure, heart rate and EMG in low level static contractions. *Acta physiologica scandinavica* **125**, 265–275.

FREYSCHUS, U. (1970). Cardiovascular adjustment to somatomotor activation. *Acta physiologica scandinavica*, suppl., 342.

GALBO, H., KJÆR, M. & SECHER, N. H. (1987). Cardiovascular, ventilatory and catecholamine response to maximal dynamic exercise in partially curarized man. *Journal of Physiology* **389**, 557–568.

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

HOLLANDER, A. P. & BOUMAN, L. N. (1975). Cardiac acceleration in man elicicted by a muscle–heart reflex. *Journal of Applied Physiology* **38**, 272–278.

HUGHES, R. & CHAPPLE, D. J. (1976). Effect on non-depolarizing neuromuscular blocking agents on peripheral autonomic mechanisms in cats. *British Journal of Anaesthesia* **48**, 56–67.

IWAMOTO, G. A. & BOTTERMAN, B. R. (1985). Peripheral factors influencing expression of pressor reflex evoked by muscle contraction. *Journal of Applied Physiology* **56**, 1676–1682.

JUHLIN-DANNFELT, A., FRISK-HOLMBERG, M., KARLSSON, J. & TESCH, P. (1979). Central and peripheral circulation relation to muscle-fibre composition in normal and hypertensive man. *Clinical Science* **56**, 335–340.

KJÆR, M., SECHER, N. H., BACH, F. W. & GALBO, H. (1987). Role of motor center activity for

hormonal changes and substrate mobilization in humans. *American Journal of Physiology* **253**, R687–695.

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.

MCALLISTER, R. G. (1979). Effect of adrenergic receptor blockade on the responses to isometric handgrip: studies in normal and hypertensive subjects. *Journal of Cardiovascular Pharmacology* **1**, 253–263.

MCCLOSKEY, D. I. (1981). Centrally-generated commands and cardiovascular control in man. *Clinical and Experimental Hypertension* **3**, 369–378.

MARTIN, C. E., SHAVER, J. A., LEON, D. F., THOMPSON, M. E., REDDY, P. S. & LEONARD J. J. (1974). Autonomic mechanisms in hemodynamic responses to isometric exercise. *Journal of Clinical Investigations* **54**, 104–115.

MITCHELL, J. H. (1985). Cardiovascular control during exercise: central and reflex neural mechanisms. *American Journal of Cardiology* **55**, D34–41.

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* **43**, 229–242.

MITCHELL, J. H., PAYNE, F. C., SALTIN, B. & SCHIBYE, B. (1980). The role of muscle mass in the cardiovascular response to static contractions. *Journal of Physiology* **309**, 45–54.

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

PATON, W. D. M. & ZAIMIS, E. J. (1951). The action of *d*-tubocurarine and of decamethonium on respiratory and other muscles in the cat. *Journal of Physiology* **112**, 311–331.

PRYOR, S. L., MITCHELL, J. H., SECHER, N. & VICTOR, R. G. (1987). Does central command increase sympathetic nerve activity in humans? *Federation Proceedings* **46**, 495.

SEALS, D. R., WASHBURN, R. A., HANSON, P. G., PAINTER, P. L. & NAGEL, F. J. (1983). Increased cardiovascular response to static contraction of larger muscle groups. *Journal of Applied Physiology* **54**, 434–437.

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

SECHER, N. H., RUBE, N. & SECHER, O. (1982). Effect of tubocurarine on human soleus and gastrocnemius muscles. *Acta anaesthesiologica scandinavica* **26**, 231–234.

SIEGEL, S. (1956). *Non parametric Statistics for the Behavioural Sciences*. Kogakusha, Tokyo: McGraw-Hill.