Pflügers Arch (1987) 408:173–177

Pflügers Archiv
European Journal of Physiology

Autonomic nervous control of the heart rate during isometric exercise in normal man

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Abstract. The relative contribution of the efferent components of the autonomic nervous system to the regulation of tachycardia induced by isometric exercise was assessed in 23 normal males. The isometric exercise (handgrip) was performed at the maximum intensity tolerated by the individual over a period of 10 s (maximal voluntary contraction – MVC) and at levels equivalent to 75, 50 and 25% of MVC for 20, 40 and 10 s, respectively. The study was performed both under control conditions and after pharmacological blockade with atropine (12 individuals) or propranolol (11 individuals). Under control conditions, the heart rate (HR) responses to isometric effort were dependent on the intensity and duration of the exercise, showing a tendency towards progressive elevation with the maintenance of muscular contraction at the levels studied. The tachycardia evoked by this effort was of considerable magnitude and of rapid onset, especially at the more intense levels of activity. Parasympathetic blockade markedly decreased tachycardia, which manifested itself during the first 10 s of exercise at all levels of intensity, whereas sympathetic blockade markedly modified the HR response after 10 s of effort at the 75 and 50% MVC levels. A slight depression of the tachycardiac response could be observed already after 10 s of maximum effort after propranolol. The present results suggest that the autonomic regulation of these responses is based on a biphasic mechanism, with the initial phase depending on the rapid withdrawal of the parasympathetic influence, followed by a marked sympathetic contribution to the induction of tachycardia after 10 s of isometric contraction or even a little before at maximum exertion.

Key words: Heart rate – Isometric exercise – Exertion – Autonomic nervous system – Atropine – Propranolol

Introduction

The pattern of heart rate response to sustained isometric exercise has been extensively studied and its characteristics have been clearly defined in man (Lind et al. 1964; Lind and McNicol 1967; Donald et al. 1967; Mitchell and Wildenthal 1974; Asmussen 1981). The elevation in heart rate is manifested very rapidly at the beginning of isometric contraction, occurring within the first 500 ms of exertion (Petro et al. 1970; Borst et al. 1972). At the same time, the magnitude of this tachycardia seems to depend directly on the relative degree of muscle tension developed (Lind and McNicol 1967; Donald et al. 1967). Furthermore, at higher muscle tension, the response does not stabilize, but a progressive increase in tachycardia occurs while contraction is maintained (Lind and McNicol 1967; Donald et al. 1967).

The relative participation of the efferent autonomic components in the regulation of the tachycardiac response evoked by static exercise still awaits full elucidation. The extremely short latency – as little as half a second – between the initiation of muscle contraction and the chronotropic response indicates that a neural mechanism mediated by reduction of vagal activity may be the primordial factor acting at the beginning of exercise (Petro et al. 1970; Borst et al. 1972). Studies using pharmacological blockade with atropine have confirmed this parasympathetic contribution (Freyschuss 1970). The available data concerning a possible sympathetic participation in the determination of the tachycardiac response evoked by isometric exercise are controversial. No appreciable contribution was detected in some studies (Freyschuss 1970; McDonald et al. 1966; Shaver et al. 1972). In contrast, Martin et al. (1974), in a study of the heart rate response to this type of effort, at 30% of maximum contraction obtained results suggesting that the inhibition of the vagal tone was the predominant mechanism during the first 30 s of exercise, whereas from that moment up to the completion of 3 min of exercise the sympathetic effector response started to prevail. This conclusion was based on the time evolution of heart rate during experiments involving simultaneous blockade of both autonomic components, since during blockade with propranolol alone the time response was similar to the control.

Thus, the present study was undertaken to assess the relative contribution of the sympathetic and parasympathetic nervous system in the efferent control of the chronotropic response to static exercise. The investigation was conducted on normal males, with exercise being executed at different levels of intensity and using selective blockade of each different division of the autonomic nervous system.

Methods

Subjects. The study included 23 normal males aged 25 to 35 years (mean = 30 years). None of them showed any evidence of cardiocirculatory abnormalities, as determined by clinical examination and laboratory tests. All subjects had normal

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electrocardiogram, chest X-rays and two-dimensional echocardiogram. Each individual gave informed consent to participate in the study.

The group consisted of individuals leading a relatively sedentary life who were not engaged in any type of regular physical training program.

Procedures. Each experimental session was held during the postabsorptive period after a light meal. None of the volunteers used any medication that might interfere with the response to the tests. On the day of the experiment, subjects were instructed not to engage in excessive physical activity.

The study was performed with the individual spontaneously breathing atmospheric air in a room maintained at a temperature of approximately 24° C.

The handgrip was performed with the volunteer in the sitting position with his right hand positioned so as to hold the handle of an isometric effort dynamometer (Tuttle et al. 1950). At the same time the individual maintained spontaneous breathing through a mouthpiece connected to a Hans Rudolph-type valve, with nasal occlusion maintained with a clamp. Then, the maximal voluntary contraction (MVC) that the individual was able to effect was determined and defined as the maximal level of exertion that could be maintained for 10 s. This value (MVC = 100%) was used to determine the remaining levels studied (75, 50 and 25% MVC).

The dynamometer used was equipped with a displacement strain-gauge (Statham 11347-G1, CA, USA) coupled to a 4-channel recorder (7754 A Hewlett-Packard, MA, USA) and to a 2-channel memory oscilloscope (Tektronix, OR, USA) which permitted the simultaneous recording of isometric contractions and cardiocirculatory variables and allowed the volunteer to follow them in the oscilloscope display. Thus, the volunteer was able to maintain exertion at constant levels as required during the different phases of the experiment. The relative levels of effort developed by the volunteer were quantified with precision thanks to the linear characteristics of the dynamometer demonstrated by an appropriate calibration system.

All individuals performed static exercise at 100, 75, 50 and 25% MVC levels for 10, 20, 40 and 10 s, respectively, in the absence of pharmacological blockade. A resting interval was permitted between tests until heart rate returned to control values. Twelve individuals were retested after peripheral intravenous administration of atropine at the dose of 0.04 mg/kg body weight injected over a period of 90 s. The remaining eleven individuals were also retested after peripheral intravenous administration of propranolol at the dose of 0.2 mg/kg body weight injected over a period of 2 min. The age range of the two groups of volunteers submitted to pharmacological blockade was superimposable. The drugs were administered with the individual in the supine position after 20 min of rest. Heart rate was monitored throughout this period and up to 5 min after drug infusion.

During the performance of static exercise, electrocardiogram, instantaneous heart rate (obtained by coupling a bipolar electrocardiographic derivation to a model 8812 A Hewlett-Packard cardiotachometer) and respiratory movements (evaluated by measuring variation in oral pressure through a lateral inlet of respiratory valve connect to a differential strain gauge) were continuously recorded starting 20 s before and up to 20 s after the completion of exertion. The volunteers were instructed not to interrupt breathing during the isometric contractions in order to avoid the occurrence of a simultaneous Valsalva maneuver.

Statistical analysis. Heart rate values were expressed as mean $\pm$ SEM calculated at 10 s intervals. The data were analyzed statistically by the Student t-test for paired samples, with the level of significance set at 5%.

Results

Heart rate response to isometric exercise without autonomic blockade

Figures 1 and 2 show the pattern of heart rate response to static exercise without autonomic blockade, which was superimposable for the two groups.

Heart rate increased appreciably during the first 10 s of exercise at all levels tested, except for 25% MVC and this increase was directly proportional to the intensity of the effort. At the levels in which effort was maintained beyond 10 s, heart rate also tended to increase, although this tendency was less marked, without reaching stabilization.

The return of heart rate to control values also occurred rapidly after the interruption of exertion. Twenty seconds after exertion, heart rate was comparable to control values regardless of the intensity of effort. The basal values of resting heart rate were different for the two groups as they are composed by different subjects (atropine: 12 individuals and propranolol: 11 individuals).

Effects of pharmacological blockade on heart rate under resting conditions

Intravenous administration of atropine sulfate to subjects resting in the supine position caused a percent increase in heart rate of 71.4 ± 5.7 ($p < 0.001$) from a basal value of 70 ± 2.0 bpm to 119 ± 3.2 bpm (mean $\pm$ SEM).

Beta-adrenergic blockade with propranolol induced a reduction of resting heart rate from a basal value of 78 ± 2.8 bpm to 64 ± 2.5 bpm ($-17.9 \pm 1.6\%$; $p < 0.001$).

Effects of parasympathetic blockade on the chronotropic response to static exercise

The tachycardia observed during the first 10 s of isometric effort was intensely depressed by parasympathetic blockade at all levels at which it occurred (Fig. 1). The mean increments observed during this period before and after blockade were 22 ± 1.8 and 4 ± 0.8 bpm ($p < 0.001$) at 100% MVC, 14 ± 1.1 and 2 ± 0.5 bpm ($p < 0.001$) at 75% MVC, and 9 ± 1.3 and 1 ± 0.5 bpm ($p < 0.001$) at 50% MVC. It should be pointed out that atropine, even though it caused a marked modification of the response during this phase of exertion, did not completely abolish the tachycardia response which, although slight, continued to be significant. The heart rate response at 25% MVC did not change after blockade, since even under control conditions there was no appreciable increase in heart rate during this time interval (control: 1 ± 0.7 bpm; atropine: -1 ± 0.4 bpm).

After 10 s of isometric effort, the increase in heart rate at 75 and 50% MVC was more discretely influenced by atropine. Between 10 and 20 s of effort, heart rate increased by 7 ± 1.7 and 3 ± 0.8 bpm ($0.05 < p < 0.1$) at 75% MVC and by 1 ± 1.1 and 1 ± 0.7 bpm ($p > 0.5$) at 50% MVC

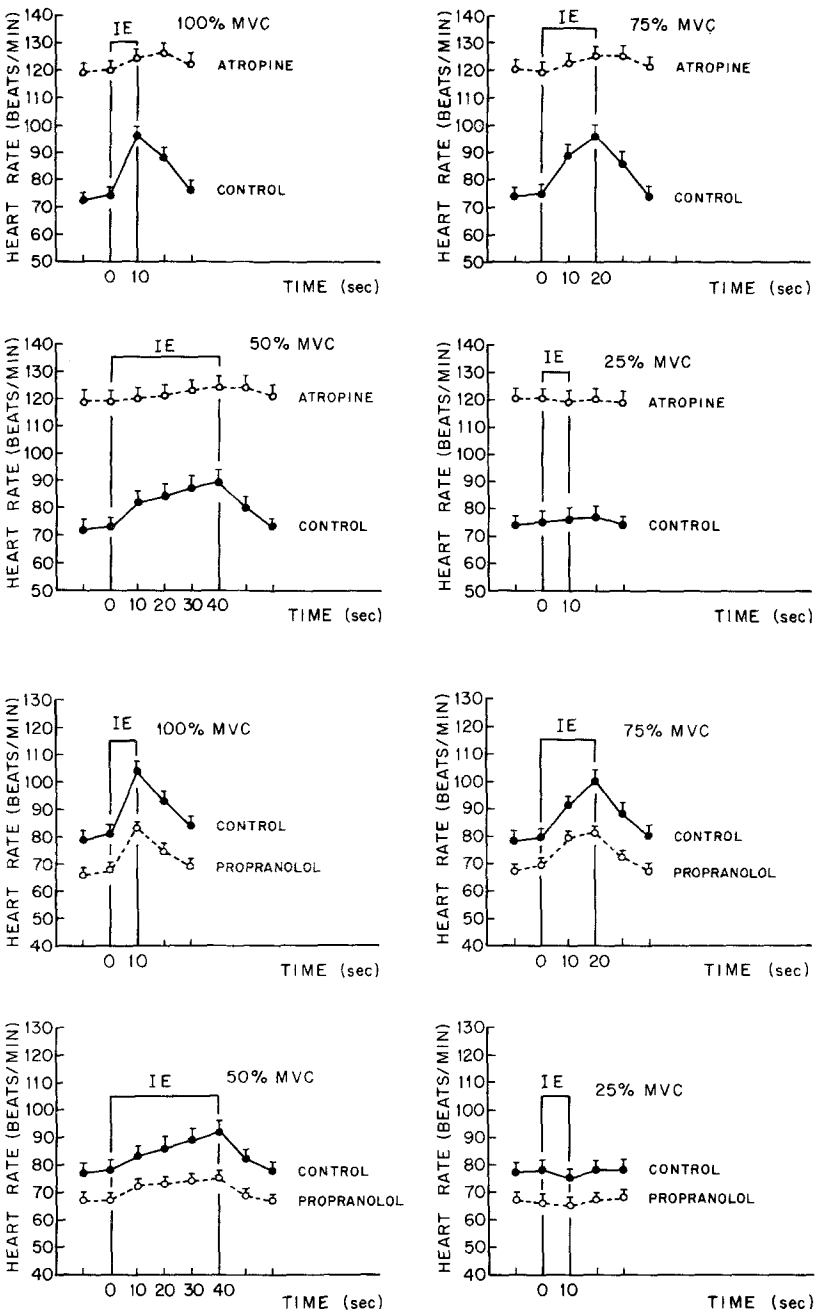

Fig. 1
Heart rate response to isometric exercise, at 100, 75, 50 and 25% of MVC, during 10, 20, 40 and 10 s, respectively, before (*congrol*) and after pharmacological blockade (*atropine*: 0.04 mg/kg body weight; $N = 12$). The values are means $\pm$ SEM at 10 s intervals. The exercise period was enclosed in *vertical bars*

Fig. 2
Heart rate response to isometric exercise, at 100, 75, 50 and 25% of MVC, during 10, 20, 40 and 10 s, respectively, before (*control*) and after pharmacological blockade (*propranolol*: 0.2 mg/kg body weight, $N = 11$). The values are means $\pm$ SEM at 10 s intervals. The exercise period was enclosed in *vertical bars*

before and after pharmacological blockade, respectively. At 50% MVC, increases of 7 ± 1.5 and 4 ± 1.4 bpm were observed between 10 and 40 s of effort before and after atropine, the difference being nonsignificant.

Effects of sympathetic blockade on the chronotropic response to static exercise

Figure 2 shows the heart rate response to isometric exercise before and after administration of propranolol at the dose of 0.2 mg/kg body weight. Sympathetic blockade did not change the tachycardiac response occurring during the initial 10 s of effort at 50 and 75% MVC. At the maximum level of effort (100% MVC), however, blockade caused a slightly lower but significant increase in heart rate. During these initial 10 s, the mean heart rate increase before and after blockade was 23 ± 3.2 and 15 ± 2.1 bpm ($p < 0.005$) at 100% MVC, 12 ± 1.9 and 10 ± 1.6 bpm ($0.05 < p < 0.1$) at 75% MVC, and 5 ± 1.1 and 5 ± 1.2 bpm ($p > 0.5$) at 50% MVC. The heart rate response at 25% MVC did not change after propranolol. However, it should be pointed out that heart rate at this level did not change significantly even under control conditions (control: -2 ± 0.9 bpm: propranolol: -1 ± 0.9 bpm).

The effect of beta-adrenergic blockade was conspicuous after 10 s of effort at 75 and 50% MVC. Between 10 and 20 s of effort at 75% MVC, heart rate underwent mean increases of 8 ± 1.6 and 2 ± 0.8 bpm ($p < 0.005$) before and after propranolol, respectively. Between 10 and 40 s of effort at 50% MVC, mean heart rate increased by 8 ± 1.9 and 2 ± 1.1 bpm ($p < 0.01$) before and after propranolol, respectively.

Thus the effect of beta-adrenergic blockade was quite evident after 10 s of static effort, but at maximum MVC, this effect was demonstrable within the first 10 s of activity.

Discussion

The heart rate responses to isometric exercise obtained in the present study on normal individuals in the absence of pharmacological blockade are, as a whole, qualitatively comparable to those reported in the literature (Lind et al. 1964; Lind and McNicol 1967; Donald et al. 1967). The magnitude of the tachycardiac response, however, cannot be compared in a simple manner with similar published studies. This because, even though there is homogeneity in the manner in which the force developed is represented (a value in relation to maximal effort), the same is not true with respect to the exact characterization of maximal voluntary effort. In the present study, it was decided to standardize the maximal voluntary contraction (MVC) as the value corresponding to the greatest force developed by the individual that could be maintained for 10 s.

Thus, under control conditions, we documented tachycardia of rapid onset and of magnitude proportional to the intensity of the effort, which showed no tendency towards stabilization with the maintenance of effort. Similarly, the return of heart rate to control values after contraction was interrupted occurred rapidly, i.e. within approximately 20 s at all levels of effort investigated. Well systematized studies had already reported that isometric muscle contraction induces and almost instantaneous acceleration of heart rate (Petro et al. 1970; Borst et al. 1972; Paulev 1973). The latency between contraction and a change in heart rate was calculated to be of the order of 0.5 s. As a function of this extremely short latency, the possible mechanisms which determine the heart rate response are postulated. By considering the reasonable evidence indicating the existence of a difference between the two efferent divisions of the autonomic nervous system with respect to the speed of the response they give when stimulated (Warner and Cox 1962; Toda and Shimamoto 1968), the present data are interpreted to reflect a decreased vagal influence on the sinus node at the beginning of isometric contraction.

In the present investigation, evaluation of the heart rate response to static effort under conditions of selective pharmacological blockade of each autonomic component disclosed aspects that permit a better understanding of the efferent mechanisms that participate in the regulation of this response. Atropine caused an appreciable reduction of the increase in heart rate occurring during the initial 10 s of exercise, whereas propranolol had a slight effect only on the response to maximal effort during the same phase. In contrast beta-adrenergic blockade obviously depressed the heart rate response after 10 s at 75 and 50% MVC, whereas atropine did not interfere significantly with the heart rate response during the same phase. Thus, the tachycardia evoked by static effort appears to be initially mediated by suppression of the parasympathetic activity on the sinus node, whereas after 10 s of contraction (or even a little before at maximal exertion is achieved) it is possible to identify an appreciable sympathetic contribution to the response pattern.

These data, which indicate a biphasic mechanism for the variation in heart rate induced by isometric effort, agree with experimental data which demonstrate a greater speed of the parasympathetic component in the modification of heart rate in relation to the sympathetic one (Warner and Cox 1962; Toda and Shimamoto 1968).

The vagal contribution to tachycardia induced by static exercise had been previously evaluated by pharmacological blockade in normal individuals (Freyschuss 1970). In that study, atropine inhibited the heart rate response when muscle contractions of varying intensity (50–90% MVC) were maintained for short periods of time (5–10 s), indicating that the initial elevation in heart rate during isometric exercise is of a parasympathetic nature.

The notable agreement demonstrated by global analysis of the present results was not present in the various studies carried out to evaluate the exact participation of the sympathetic component in the regulation of the chronotropic response induced by static effort. Even though significant elevations of plasma catecholamine levels were detected during static muscle contraction (Koslowski et al. 1973; Vecht et al. 1978), controversial results were obtained in the studies carried out to assess the sympathetic contribution by beta-adrenergic blockade. Data published by Freyschuss (1970) showed no change in the magnitude of the response after intravenous administration of propranolol at the dose of 10 mg, although it should be pointed out that the isometric contractions studied were of short duration (5–10 s) and that only one individual was investigated McDonald et al. (1966), in a study of the systemic circulatory response to isometric exercise at 30% MVC, found that the percent increase in heart rate at the end of 5 min of effort under the action of propranolol was significantly higher than under control conditions. Results published by Martin et al. (1974) also showed vagal participation in the initial phase of tachycardia associated with isometric exercise at 30% MVC, since atropine reduced the increase in heart rate during the initial 30 s of muscle contraction but did not interfere with the response thereafter. In the same study, administration of propranolol alone did not change the pattern of heart rate variation of any phase of the 3-min exertion test. However, on the basis of the observation that simultaneous blockade of the two components practically suppressed the tachycardia elicited by exercise, these authors concluded that there is a sympathetic mechanism that participates in this response and that this mechanism becomes operant after the initial utilization of the vagal mechanism.

The present results are also compatible with the interpretation of a participation of the sympathetic component in the regulation of the tachycardiac response evoked by static effort. This participation was demonstrable after 10 s at 75 and 50% MVC, and a little before at maximal exertion in the presence of beta-adrenergic blockade.

Isometric exercise has been utilized as a test of autonomic activity (Ewing et al. 1974; Nazar et al. 1975; Marin Neto et al. 1986), with effort levels of about 30% MVC being commonly used for a period of approximately 3 min. However, in view of the results obtained in the present study, the use of effort levels above 50% MVC seems to be more recommendable, since the responses evoked by muscle contraction appear to be more intense and are able to activate both efferent autonomic components within a shorter period of time. Furthermore, maximal effort and effort corresponding to 75% MVC, when exerted for 5–10 s, can be considered to induce a heart rate response

depending almost exclusively on the mechanism of vagal release. Thus, these levels may be used as adequate tests for the evaluation of parasympathetic action on the sinus node (Maciel et al. 1985).

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Received May 28/Accepted September 18, 1986