Eur J Appl Physiol (1993) 66:202–206

European Journal of Applied Physiology and Occupational Physiology

Autonomic nervous control of heart rate during blood-flow restricted exercise in man

J. C. L. Sun[1], O. Eiken[2], and I. B. Mekjavic[1]

[1] School of Kinesiology, Simon Fraser University, Burnaby, British Columbia, Canada V5A 1S6
[2] Department of Clinical Physiology, Huddinge Hospital, 141 86 Huddinge, Sweden

Accepted October 10, 1992

Summary. Power spectra of instantaneous heart rate (f_c) allows the estimation of the contribution of sympathetic and parasympathetic control of f_c during steady-state conditions. The present study was designed to examine autonomic control of f_c as influenced by normal dynamic leg exercise and by ischemic leg exercise. Eight subjects performed supine cycle ergometry at 30% of their control peak work rate, with and without blood-flow restriction. Blood-flow restriction was induced by exposing the exercising legs to a supra-atmospheric pressure of 6.7 kPa (leg positive pressure; LPP). The exercise responses of arterial pressure and f_c increased ($P<0.05$) by LPP exposure. The exaggerated pressor response may be attributed to a chemoreflex drive originating in the ischemic muscles. Exposure to LPP during exercise also produced a significant decrease in parasympathetically mediated high frequency (HF; 0.15–1.00 Hz) fluctuation of f_c, as indicated by a decrease ($P<0.05$) in percent HF power compared to the control exercise level. During LPP exercise, the sympathetically mediated very low frequency (VLF; 0–0.05 Hz) fluctuation of f_c increased, as indicated by an increase ($P<0.05$) in percent VLF power above control exercise levels. Both LPP and control exercise conditions decreased ($P<0.05$) power in all frequency ranges of interest compared to their respective resting conditions. The results suggest that the increase in f_c associated with normal dynamic exercise was mediated predominantly by parasympathetic withdrawal, whereas the exaggerated f_c response during ischemic exercise resulted from a combination of cardiac sympathetic drive and parasympathetic withdrawal. The increase in sympathetic activity is attributable to a muscle chemoreflex drive, which also may have attenuated parasympathetic activity by reciprocal inhibition. Alternatively, augmented central command mediated parasympathetic withdrawal during ischemic exercise.

Correspondence to: I. B. Mekjavic

Key words: Power spectra of instantaneous heart rate – Sympathetic nervous activity – Parasympathetic nervous activity – Ischemic muscle exercise

Introduction

Blood flow restriction to the exercising muscles results in compensatory cardiovascular responses which act to increase arterial pressure and hence to reduce blood-flow deficit in the working muscles. This exaggerated exercise pressor response is brought about by increases in heart rate (f_c) and total peripheral resistance and is mediated by the muscle chemoreflex (for review see Mitchell and Schmidt 1983) and possibly by augmented central command (Victor and Seals 1989). In humans, performing dynamic leg exercise, moderate restrictions of blood flow in the working muscles lead to exaggerated f_c and arterial pressure response even during mild exercise (Eiken and Bjurstedt 1987).

Information is scarce regarding efferent nervous mechanisms eliciting such ischemically induced f_c increases in exercising man. Judging from experiments in animals, activation of muscle chemosensors may result in sympathetic stimulation of the heart (Wildentahl et al. 1968; Mitchell et al. 1977). Increases in exercise f_c governed by central command appear to be mediated by parasympathetic withdrawal (Victor et al. 1989). Under conditions of unrestricted muscle blood flow, f_c increases associated with mild to moderate dynamic exercise in man are attributable mainly to parasympathetic withdrawal, sympathetic chronotropic stimulation of the heart being less significant or even absent (Robinson et al. 1966; Galbo 1983; Orizio et al. 1988; Yamamoto et al. 1991).

Therefore, it was thought to be of interest to investigate the effect of muscle blood-flow restriction on autonomic control of f_c during low-intensity exercise. Graded blood-flow restriction in exercising muscles was induced by applying a supra-atmospheric pressure to the legs during supine cycling using a method described by

Eiken and Bjurstedt (1987). The autonomic nervous mechanisms controlling f_c were investigated by use of power spectral analysis of instantaneous f_c (R-R interval). This non-invasive method is a useful tool to provide insight into sympathetic/parasympathetic control of f_c. The use of power spectral analysis to deduce autonomic balance and autonomic control of f_c has been validated by use of pharmacological blocking agents (Akselrod et al. 1985; Pomeranz et al. 1985; Pagani et al. 1986) and de-innervation (Pagani et al. 1986). Characteristic changes in power spectra of instantaneous f_c, associated with autonomic nervous changes controlling f_c, occur during exercise at different intensities (Arai et al. 1989; Perini et al. 1990; Yamamoto et al. 1991).

Specifically, the power spectra of instantaneous f_c yield three major components in the following ranges: 0–0.05 Hz, 0.05–0.15 Hz, 0.15–1.00 Hz (Akselrod et al. 1981, 1985; Perini et al. 1990), defined as the very low frequency (VLF), low frequency (LF) and high frequency (HF) ranges, respectively. Whereas the sympathetic system contributes to f_c variations at frequencies less than 0.12 Hz (Akselrod et al. 1981, 1985; Pomeranz et al. 1985), the parasympathetic system mediates f_c fluctuations predominantly in the HF range (Akselrod et al. 1981, 1985; Pomeranz et al. 1985). Applying this analytical approach we examined the contribution of the sympathetic and parasympathetic nervous system in the exaggerated exercise f_c response during muscle ischemia.

Methods

Subjects. Nine male subjects participated in this study. None of the subjects had a history of cardiovascular disease and all were considered healthy. Their mean (and range) age, height and mass were 28 (23–35) years, 1.73 (1.67–1.78) m and 70 (63–81) kg, respectively. All subjects were briefed about the experimental procedures and were familiarized with the protocol, prior to the experiments. The protocol was approved by the Institutional Ethics Review Committee.

Experimental arrangements. The experimental arrangements that were used to induce graded blood-flow restriction during exercise have been described by Eiken and Bjurstedt (1987). Briefly, the experiments were conducted with the subject positioned supine in the opening to a pressure chamber, with the legs inside the chamber and the feet strapped to the pedals of a mechanically braked cycle ergometer (Monark). The axis of the pedals was positioned at the same level as the heart. Sealing of the chamber was accomplished by using a rubber diaphragm with holes and short self-sealing sleeves for the legs. The subject was provided with shoulder supports to avoid the subjects being pushed out of the chamber as the pressure in it was increased.

Instrumentation. Electrocardiographic (ECG) recordings were obtained from pre-gelled electrodes positioned in a standard lead II arrangement, using an electrocardiograph (Fukuda Denshi, FD-13). The continuous ECG signal was recorded on magnetic tape using a tape recorder (Hewlett Packard, 3968A), for subsequent analysis.

Systolic arterial pressure (P_{as}) was measured using an automatic sphygmomanometric blood-pressure recorder (UA-251, Japan). Diastolic arterial pressure (P_{ad}) was measured by the volume-clamp technique (Penaz 1973) using a Finapres 2350 (Wesseling et al. 1982). The arm and finger, from which arterial pressure measurements were made, were supported by a platform at the same level as the heart. P_{as} and P_{ad} were determined by different methods because, during muscular exercise, P_{as} but not P_{ad} is measured accurately by the sphygmomanometrical method (Kaijser 1987), whereas P_{ad} but not P_{as} is measured accurately by the Finapres (Idema et al. 1989). Mean arterial pressure ($\bar{P}$) was calculated by adding one third of the pulse pressure to the P_{ad}.

Experimental protocol. Prior to the experiments, each subjects' work capacity was established, once with normal atmospheric pressure in the chamber (control) and once with a supra-atmospheric chamber pressure of 6.7 kPa (leg positive pressure; LPP). The two trials were separated by a minimum of 48 h and conducted in random order. Each trial started with 4 min of loadless pedaling after which the work rate was increased by 30 W every 2 min until the subject was unable to maintain the prescribed work rate. Peak work rate was defined as the highest work rate that the subject could sustain for the full 2-min period.

This incremental-load exercise performed in the control condition was solely for the purpose of establishing individual work rates equivalent to 30% of peak work rate. The additional incremental-load exercise performed at supra-atmospheric pressure (LPP) enabled us to establish the corresponding relative work rate in the LPP condition.

All subjects were investigated in four steady-state conditions: control rest, control exercise, LPP rest and LPP exercise. Each subject performed one control and one LPP (6.7 kPa) experiment in a random order. The experiments were separated by a minimum of 48 h. Each experiment consisted of 14 min of motionless rest followed by 14 min of constant-load pedaling at 30% of individual control peak work rate. In the LPP condition this work rate represented 43% (range: 40–50%) of the LPP peak work rate. P_{as} and P_{ad} were measured periodically, whereas ECG was recorded continuously throughout the experiments.

Data analysis. For each subject and condition (control rest, LPP rest, control exercise and LPP exercise) 14 min of continuous pre-recorded ECG signals were examined for substantial baseline drifts, discontinuities and other noticeable artifacts. This screening process provided clear and continuous ECG signals for R-R interval extraction.

ECG analysis and R-R interval extraction was accomplished with data acquisition software (LabVIEW 2, National Instruments) and hardware (NB-A2000, National Instruments) using a computer (Macintosh II, Apple). An R-R interval tachogram was derived from over 500 consecutive R-R intervals obtained for each subject within the last 10 min of the 14 min rest and constant rate exercise periods. After removal of the DC bias and normalization of the tachograms (divided by mean R-R; as suggested by Akselrod et al. 1985), the data were smoothed using a Hanning window and subsequently sampled at 10 Hz, from which fast Fourier transform based power spectra were derived.

Power spectral frequencies between 0 and 0.05 Hz were defined as the VLF, between 0.05 and 0.15 Hz as the LF, and between 0.15 and 1.00 Hz as the HF (Perini et al. 1990). Integration of the power spectrum within these limits yielded quantitative measures of normalized VLF, LF and HF power. The integral of power from 0 to 1.00 Hz was defined as the total normalized power and VLF, LF and HF power were also expressed as a percentage of total power (% VLF, % LF and % HF; Perini et al. 1990). The LF : HF ratio was calculated in an attempt to derive a quantitative indication of sympathetic/parasympathetic balance (Pagani et al. 1986).

A two-way analysis of variance was performed on the data, to test whether the effects of exercise, LPP and their interaction significantly affected f_c fluctuations in the defined frequency ranges.

Results

At rest, P_{as} was higher ($P<0.05$) in the LPP [mean (SD); 17.73 (2.27) kPa] than in the control [15.86 (1.20) kPa] condition. Resting values for $\bar{P}$ did not differ significantly between the LPP [13.43 (1.47) kPa] and control [11.97 (1.06) kPa] conditions. Likewise, resting P_{ad} was similar in the LPP [11.33 (1.73) kPa] and control [10.00 (1.47) kPa] conditions. As expected, all arterial blood pressure (P_a) values increased ($P<0.05$) with the transition from rest to steady-state exercise in both the control and LPP conditions. This exercise-induced increase in P_a was greater in the LPP condition. During exercise P_{as} was 4.13 kPa higher ($P<0.01$) in the LPP [23.86 (1.87) kPa] than in the control [19.60 (1.73) kPa] condition. Likewise, LPP increased ($P<0.01$) exercise values for $\bar{P}$ from [13.47 (1.46) kPa] to [17.06 (1.60) kPa] and for P_{ad} from [11.33 (1.73) kPa] to [13.60 (2.00) kPa].

At rest, f_c attained similar values in the control [63 (10) min^{-1}] and the LPP [67 (9) min^{-1}] conditions. During exercise f_c was higher ($P<0.05$) in the LPP [111 (16) min^{-1}] than in the control [102 (12) min^{-1}] condition.

Total normalized power was unaffected by LPP exposure both at rest and during exercise. Exercise induced a decrease in total power of 5.5×10^{-2} ($P<0.001$) from a resting value of 0.099 (0.052) to 0.044 (0.023) during the control condition. A similar exercise induced decrease of 5.5×10^{-2} ($P<0.001$) from a resting value of 0.103 (0.048) to 0.047 (0.027) was observed during the LPP condition.

Normalized power within the VLF, LF and HF ranges was unaffected by LPP both at rest and during exercise. Exercise induced a decrease in power within all frequency ranges, during the control and LPP conditions. Exercise decreased VLF power from resting values of 0.057 (0.034) and 0.050 (0.036) to 0.025 (0.016) and 0.034 (0.023) ($P<0.05$) during the control and LPP conditions, respectively. LF power decreased from resting values of 0.034 (0.021) and 0.039 (0.015) to 0.014 (0.012) and 0.010 (0.008) ($P<0.001$) upon exercise in the control and LPP conditions, respectively. Exercise decreased HF power from resting values of 0.008 (0.006) and 0.012 (0.008) to 0.005 (0.005) and 0.003 (0.003) ($P<0.01$) in the control and LPP conditions, respectively (Fig. 1).

In the control condition the transition from rest to exercise did not affect values of %VLF, %LF and %HF power. However, exercise during the LPP condi-

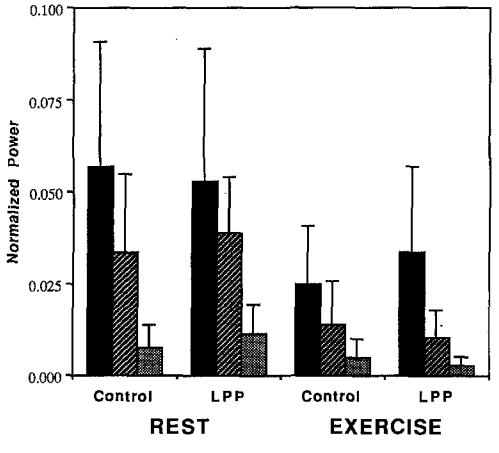

Fig. 1. Mean normalized very low frequency (VLF, ■), low frequency (LF, ▨) and high frequency (HF, ▩) power (standard deviations) during the four experimental conditions. Normalized VLF, LF and HF power were derived by integration of the power spectrum within the defined frequency limits. Power was multiplied by a factor of 10^5 ($n=9$)

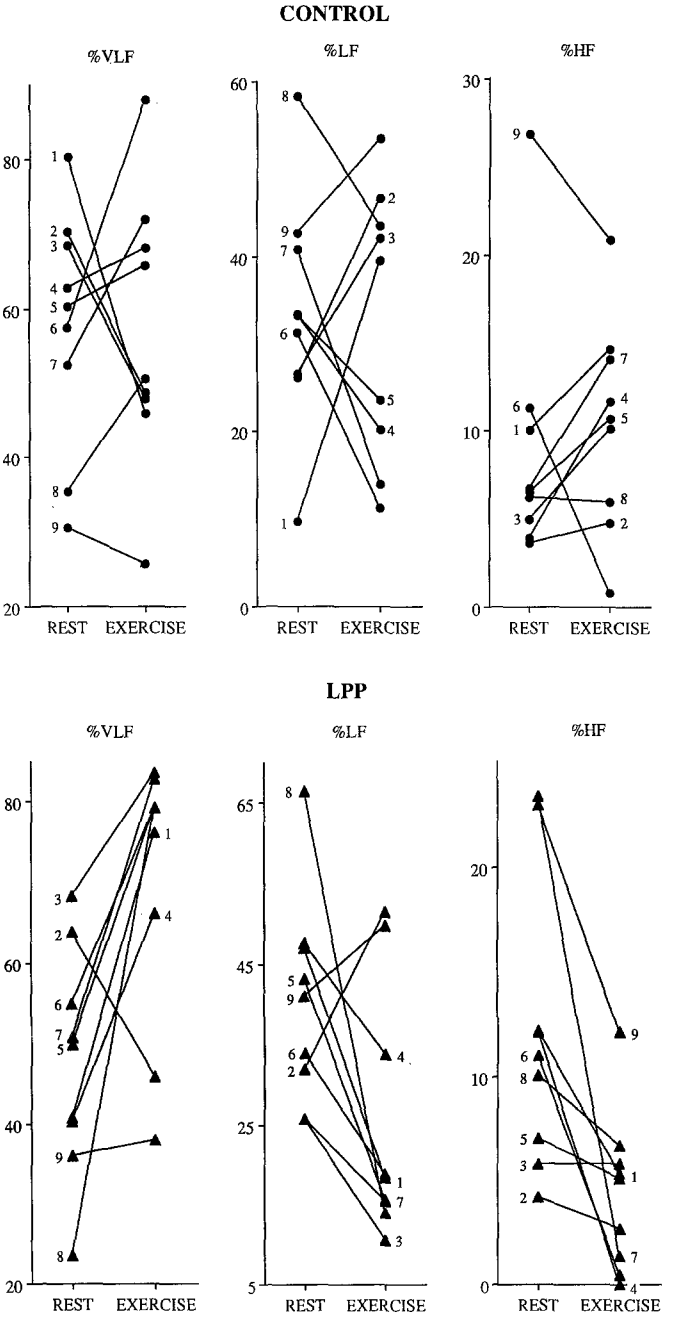

Fig. 2. Changes of %VLF, %LF and %HF power from rest to exercise for each subject during the control (*top*) and leg positive pressure (*LPP*) (*bottom*) conditions. Percent power (% power) was derived by expressing normalized VLF, LF and HF power as a percentage of total power ($n=9$)

tion increased % VLF power by 1.5 fold ($P<0.05$) from a resting value of 47.6 (14.1) % to 70.1 (16.8) % as well as decreased % HF power by 2.6 fold ($P<0.05$) from a resting value of 12.1 (6.9) % to 4.6 (3.6) %. % LF power was unaffected by exercise during the LPP condition. At rest, exposure to LPP did not affect percent power within any of the frequency ranges. However, during exercise, exposure to LPP elevated % VLF power from the control value of 57 (18.3) % by 1.2 fold ($P<0.05$) and decreased % HF power by 2.3 fold ($P<0.05$) from the control value of 10.4 (6.0) %. % LF power was unaffected by LPP during exercise (Fig. 2).

LF : HF ratio attained similar values in all four experimental conditions, control rest [5.3 (3.0)], LPP rest [4.3 (2.1)], control exercise [5.2 (4.6)] and LPP exercise [6.7 (6.0)]. However, there was increased inter-subject variability (as indicated by larger standard deviations) during exercise in both the control and LPP conditions.

Discussion

Exposure of the legs to increased ambient pressure during cycle exercise is an effective method to reduce local perfusion pressure, which, at LPP of 6.7 kPa, results in a moderate reduction of blood flow in the exercising leg muscles (Eiken 1987). Examination of mean f_c and P_a as well as the power spectrum of instantaneous f_c fluctuation (R-R interval spectrum) provides insight into the effect of muscle ischemia on autonomic nervous mechanisms mediating cardiovascular exercise responses.

In our study, the muscle chemoreflex was activated by LPP during exercise, as evidenced from the exaggerated exercise responses for P_a and f_c in this condition. LPP exposure induced a slight increase in P_{as} at rest, which is attributable to the increased stroke volume resulting from pressure-induced displacement of blood volume from the legs to the thorax; exercise stroke volume is unaffected by LPP (Eiken and Bjurstedt 1987).

Total power of the R-R interval spectrum decreased by approximately a factor of 2 upon exercise in both the LPP and control conditions. The decrease in power occurred in all defined frequency ranges between 0 and 1 Hz (Fig. 1) and reflects an overall decrease in R-R interval fluctuation about the mean. This is in agreement with previous investigations in which total power has been reported to decrease progressively with increasing exercise intensity (Arai et al. 1989; Perini et al. 1990; Yamamoto et al. 1991). The exercise tachycardia at intensities less than approximately 30% maximum oxygen consumption is predominantly mediated by parasympathetic (vagal) withdrawal (Robinson et al. 1966; Galbo 1983; Orizio et al. 1988). A decrease in parasympathetic activity would account for the reduction in VLF, LF and HF power and hence total power, primarily because the parasympathetic system mediates fluctuations of f_c within these frequency ranges (Akselrod et al. 1981; Pomeranz et al. 1985).

Our results showed that exposure to LPP during exercise increased % VLF power and decreased % HF power compared to control exercise values. This may indicate that cardiac sympathetic drive and parasympathetic withdrawal are enhanced by blood-flow restriction in the working muscles. The slow responding sympathetic system mediates f_c fluctuation at frequencies less than approximately 0.12 Hz (Akselrod et al. 1981, 1985; Pomeranz et al. 1985), whereas HF fluctuation of f_c is predominantly mediated by the fast responding parasympathetic system (Akselrod et al. 1981, 1985; Pomeranz et al. 1985). The increase in the share of the power spectrum contributed by VLF f_c fluctuation occurring during muscular exercise has been attributed to increased sympathetic drive (Perini et al. 1990).

That cardiac sympathetic drive was increased during LPP exercise may reflect activation of the muscle chemoreflex, since stimulation of muscle chemosensors activates cardiac sympathetic efferents (Wildenthal et al. 1968; Mitchell et al. 1977). However, the notion that the exaggerated f_c response observed during ischemic exercise in man is mediated by the muscle chemoreflex has recently been challenged by Victor and Seals (1989), who proposed that this f_c response is caused by augmented central command. However, exercise f_c increases governed by central command are almost solely attributable to parasympathetic withdrawal (Victor et al. 1989) and hence cannot explain the increased sympathetic activity observed in the present LPP experiments. Thus, our results suggest that, even during low-intensity exercise, moderate restriction of muscle blood flow induces a cardiac sympathetic drive which is mediated by chemosensors in the ischemic muscles. Stimulation of muscle chemosensors may not only increase cardiac sympathetic activity but has also been found to increase muscle sympathetic nerve activity (Mark et al. 1985).

Such an increase in sympathetic activity could also reduce parasympathetic influence on f_c by inhibiting parasympathetic pathways, either centrally or peripherally. The proportionately greater parasympathetic withdrawal during LPP exercise may either be mediated by augmented central command, or may be secondary to increased sympathetic activity. This proposed reciprocal inhibition of sympathetic and parasympathetic pathways has been demonstrated by Schwartz et al. (1973) and Levy (1984). Stimulation of afferent cardiac sympathetic fibers produced an increase in cardiac sympathetic activity while simultaneously inhibiting the activity of the parasympathetic vagal fibers (Schwartz et al. 1973), whereas increasing vagal activity attenuated cardiac sympathetic activity (Levy 1984). Corroboratively, peripheral chemoreceptor stimulation has also been shown to reduce the vasodilating effect of vagal cardiac afferent stimulation (Wennergren et al. 1976). Although these findings do not directly pertain to our findings, they indicate that a reciprocal inhibitory relationship exists between the sympathetic and parasympathetic systems. It is conceivable that a similar inhibitory effect on cardiac parasympathetic activity could occur through increased group III and IV activity originating in ischemic muscles.

It should be noted that, irrespective of the underlying mechanisms, the stimulus inducing increases in cardiac sympathetic drive and parasympathetic withdrawal dur-

ing LPP exercise was strong enough to overcome the opposing effects of augmented arterial baroreceptor stimulation. Thus, P_{as} and consequently arterial baroreflex stimulation was greater during LPP exercise than during control exercise. The sensitivity of the carotid baroreflex is higher during blood-flow-restricted exercise than both at rest and during control exercise (Eiken et al. 1992).

In our study, the LF:HF ratio was examined as an index of sympathetic/parasympathetic balance (Pagani et al. 1986). Our findings seem to indicate that the LF:HF ratio changes very little between control rest and control exercise conditions, reflecting a proportionate decrease of the LF and HF power. This would be the case when parasympathetic withdrawal predominantly occurs. LF:HF ratio during LPP exercise tended to increase, although not significantly, indicating a proportionately greater increase in sympathetic activity. However, because of the intersubject variability in the LF:HF ratio, especially during exercise, the ratio is a questionable indicator of autonomic balance during exercise. Similar conclusions were drawn by Perini et al. (1990) and Arai et al. (1989). They concluded that the LF:HF ratio was not valid during exercise.

Power spectral analysis of instantaneous f_c has provided a non-invasive insight into the autonomic control of f_c. The results confirm that increases in f_c during low intensities of supine exercise are predominantly mediated by parasympathetic withdrawal. It also suggests that the exaggerated exercise response for f_c induced by muscle ischemia is the result of an increased cardiac sympathetic activity, which probably simultaneously inhibits parasympathetic (vagal) activity.

Acknowledgements. We would like to thank Dr. K. Mita, K. Akataki, K. Ito and M. Walsh for their assistance in our study. The study was supported by a grant from the Natural Sciences and Engineering Research Council (NSERC). J. C. L. Sun was a recipient of an NSERC undergraduate scholarship.

References

Akselrod S, Gordon D, Ubel FA, Shannon DC, Barger AC, Cohen RJ (1981) Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat-to-beat cardiovascular control. Science 213:220–222

Akselrod S, Gordon D, Madwed JB, Snidman NC, Shannon DC, Cohen RC (1985) Hemodynamic regulation: investigation by spectral analysis. Am J Physiol 256:H867–H875

Arai Y, Saul JP, Albrecht P, Hartley LH, Lilly LS, Cohen RJ, Colucci WS (1989) Modulation of cardiac autonomic activity during and immediately after exercise. Am J Physiol 256:H132–H141

Eiken O (1987) Responses to dynamic leg exercise in man as influenced by changes in muscle perfusion pressure. Acta Physiol Scand 131 [Suppl 566]

Eiken O, Bjurstedt H (1987) Dynamic exercise in man as influenced by experimental restriction of blood flow in the working muscles. Acta Physiol Scand 131:339–345

Eiken O, Convertino VA, Doerr DF, Dudley GA, Morariu G, Mekjavic IB (1992) Interaction of the muscle chemoreflex and the carotid baroreflex in man during exercise. Acta Physiol Scand 144:325–331

Galbo H (1983) Hormonal and metabolic adaptation to exercise. Thieme, Stuttgart

Idema RN, Van Den Meiracker AH, Imholz PBM, Man In't Veldt AJ, Settels JJ, Ritsema Van Eck HJ, Schalenkamp MADH (1989) Comparison of Finapres non-invasive beat-to-beat finger blood pressure with intrabrachial artery pressure during and after bicycle ergometry. J Hypertens 7 [Suppl 6]:558–559

Kaijser L (1987) The indirect method of recording blood pressure during exercise - can the diastolic pressure be measured? Clin Physiol 7:175–179

Levy MN (1984) Cardiac sympathetic-parasympathetic interactions. Fed Proc 43:2598–2602

Mark AL, Victor RG, Nerhed C, Wallin BG (1985) Microneurographic studies of the mechanisms of sympathetic nerve responses to static exercise in humans. Circ Res 57:461–469

Mitchell JH, Schmidt RF (1983) Cardiovascular reflex control by afferent fibres from skeletal muscle receptors. In: Shepherd JT, Abboud FM (eds) Handbook of Physiology, sect 2. The cardiovascular system, vol III. American Physiological Society, Washington, DC, pp 623–658

Mitchell JH, Reardon WC, McCloskey DI (1977) Reflex effects on circulation and respiration from contracting skeletal muscle. Am J Physiol 233:H374–H378

Orizio C, Perini R, Comande A, Castellano M, Beschi M, Veicsteinas A (1988) Plasma catecholamines and heart rate at the beginning of muscular exercise in man. Eur J Appl Physiol 57:644–651

Pagani M, Lombardi F, Guzzetti S, Rimoldi O, Furlan R, Pizzinelli P, Sandrone G, Malfatto G, Dell'orto S, Piccaluga E, Turiel M, Baselli G, Cerutti S, Malliani A (1986) Power spectral analysis of heart rate and arterial pressure variabilities as a marker of sympatho-vagal interaction in man and conscious dog. Circ Res 59:178–193

Penaz J (1973) Photoelectric measurement of blood pressure, volume and flow in the finger. In: Digest of the International Conference on Medicine and Biological Engineering. Dresden Conference Committee of the 10th International Conference on Medicine and Biological Engineering, p 104

Perini R, Orizio C, Baselli G, Cerutti S, Veicsteinas A (1990) The influence of exercise intensity on the power spectrum of heart rate variability. Eur J Appl Physiol 61:143–148

Pomeranz B, Macaulay RJB, Caudill MA, Kutz I, Adam D, Gordon D, Kilborn KM, Barger AC, Shannon DC, Cohen RJ, Benson H (1985) Assessment of autonomic function in humans by heart rate spectral analysis. Am J Physiol 248:H151–H153

Robinson BF, Epstein SE, Beiser GD, Braunwald E (1966) Control of heart rate by the autonomic nervous system. Circ Res 19:400–411

Schwartz PJ, Pagani M, Lombardi F, Malliani A, Brown AM (1973) A cardio-cardiac sympathovagal reflex in the cat. Circ Res 32:215–221

Victor RG, Seals DR (1989) Reflex stimulation of sympathetic outflow during rhythmic exercise in humans. Am J Physiol 257:H2017–H2024

Victor RG, Pryor SL, Secher NH, Mitchell JH (1989) Effects of partial neuromuscular blockade on sympathetic nerve responses to static exercise. Circ Res 65:468–476

Wennergren G, Little R, Oberg B (1976) Studies on the central integration of excitatory chemoreceptor influences and inhibitory baroreceptor and cardiac receptor influences. Acta Physiol Scand 96:1–18

Wesseling KH, De Wit B, Settles JJ, Klawer WH (1982) On the indirect registration of finger blood pressure after Penaz. Funct Biol Med:245–250

Wildenthal K, Mierzwak DS, Sheldon Skinner N Jr, Mitchell JH (1968) Potassium-induced cardiovascular and ventilatory reflexes from the dog hindlimb. Am J Physiol 215:542–548

Yamamoto Y, Hughson RL, Peterson JC (1991) Autonomic control of heart rate during exercise studied by heart rate variability spectral analysis. J Appl Physiol 71:1136–1142