

Giosuè Gulli
Antonio Cevese
Paola Cappelletto
Gianpaolo Gasparini
Federico Schena

Moderate aerobic training improves autonomic cardiovascular control in older women

Received: 19 July 2002
Accepted: 20 December 2002

G. Gulli, M. D., Ph. D. · A. Cevese, M. D. ·
P. Cappelletto, B. S. · G. Gasparini, M. D. ·
F. Schena, M. D., Ph. D.
Dept. of Neurological Science and Vision
Section of Physiology
University of Verona
Verona, Italy

F. Schena, M. D., Ph. D.
CeBiSM
Research Center of Bioengineering & Motor
Sciences
Rovereto, Italy

Giosuè Gulli, M. D., Ph. D. (✉)
Neurophysiology Clinic
Dept. of Neurology
University of Erlangen-Nuremberg
Schwachbachanlage 6
91054 Erlangen, Germany
Tel.: +49-91 31/8 53-60 06
Fax: +49-91 31/8 53-48 46
E-Mail:
giosue.gulli@neuro.med.uni-erlangen.de

■ **Abstract** The decline in the cardiovascular autonomic regulation in advanced age is considered a risk factor for several cardiovascular diseases. We tested, on eleven healthy untreated women aged 60–70 years, whether a six-month period of group-based training exerts positive effects on this age-associated decline.

Before and after training, ECG and arterial pressure (Finapres) were recorded in supine position. We calculated mean values \pm SEM of R-R period (RR), systolic (SAP) and diastolic (DAP) arterial pressure, as well as, by autoregressive spectral analysis methods, low (≈ 0.1 Hz) and high (respiratory) frequency oscillations of RR (LF_{RR} , HF_{RR}) and SAP (LF_{SAP} , HF_{SAP}), and the baroreflex sensitivity (BRS). Training induced statistically sig-

nificant changes ($p < 0.05$ by paired *t*-test): increase in RR (mean \pm SEM) from 894 ± 41 to 947 ± 31 ms and in heart rate variability (HRV) by 25 %, decrease in DAP from 75.8 ± 3.0 to 70.8 ± 2.2 mmHg, no change in SAP. LF_{RR} and LF_{SAP} increased by more than 100 %, while BRS by 32 %. We suggest that the increase in BRS might be responsible for the observed bradycardia and higher LF_{RR} . An improved modulation, rather than an increase, in tonic sympathetic activity, is also suggested. A specific program of moderate aerobic training is adequate to increase the BRS and the HRV in older women.

■ **Key words** exercise · autonomic function · heart rate variability · ageing population · baroreflex

Introduction

It has been well documented that the autonomic nervous system progressively degenerates with advancing age, contributing to overall functional impairment in the elderly [16]. This degenerative process consists in a reduction of the adrenergic modulation and in an altered tonic and reflex parasympathetic cardiovascular control [32].

The autonomic cardiovascular control can be studied by the analysis of the heart rate variability (HRV) and of the arterial pressure fluctuations, either in the time or in the frequency domain. Frequency-domain analysis has

also been used for a non-invasive assessment of baroreflex sensitivity (BRS) [21, 39].

It has been shown that the prevalence of cardiovascular diseases increases with age, and it sharply rises after menopause in women [13, 24]. The morbidity and mortality rate of several cardiovascular disorders have been frequently related to reductions in heart rate variability and baroreflex sensitivity [17, 31, 46]. Moreover, a reduced cardiovascular BRS increases the risk of ventricular tachyarrhythmias and sudden cardiac death in the presence of myocardial ischemia [3, 7]. Finally, the combination of reduced values of these two markers provides additional prognostic value to that of either marker alone [30]. Since these are common findings in

the elderly, it is reasonable to study the beneficial effects of exercise and the physiological mechanisms in eliminating or reducing such cardiovascular risk factors. Recently it has been shown that regular aerobic exercise improves BRS in old men [36]. However, whether in postmenopausal women, in whom the cardiovascular degeneration due to the normal aging process is associated to the menopausal estrogenic loss, a regular physical activity program may be effective, is still under investigation [10, 11].

In the elderly population it is also necessary to assess the proper intensity of an exercise-training program, in order to keep the physical loads at minimal, although effective, levels. Unquestionably, heavy workloads in the elderly can bear cardiovascular and locomotor hazardous consequences. Moreover the adherence to physical activity programs among the elderly is strongly related to psychosocial aspects, leading to better results while exercising in a group situation [6].

In the present investigation we test the hypothesis that a group-exercise program, especially designed for the aged population, is able to delay, or even reverse, the age- and hormonal loss-associated decline in cardiovascular autonomic functions, in healthy postmenopausal women. To test this hypothesis we performed spectral- and cross-spectral analysis of cardiovascular variables on a group of 60–70 year aged women, before and after a 6-month period of moderate group-exercise training.

Methods

The research was completed in 11 women (mean age 64 ± 3.8 years; body mass index 24.8 ± 1.9). We selected the subjects among those participating in the “Third Age Project”, an exercise based program of health promotion organized by the Civic Administration of Verona [6]. All subjects were previously evaluated by a complete physical examination, which was performed in the same room where the recordings took place in the following days. Exclusion criteria were hypertension ($> 140/90$ mmHg), obesity (body mass index > 30) and history of smoking and hormone replacement therapy. Of the 15 women initially accepted, we further excluded four because they were taking cardiovascular and/or autonomic effective drugs or because they did not reach the target level of training ($< 80\%$ of attendance at the gym lessons).

The study conforms to the declaration of Helsinki, and was approved by the local Ethics Committee. The nature, purpose and risks of the study were explained to each subject before they gave written informed consent.

■ Experimental protocol

The records of cardiovascular variables, as specified below, were performed between 9:30 and 12:30 a. m., at least 3 h after a light breakfast, in a quiet room kept at constant temperature (23°C). A 10-min record was taken while the subjects laid quietly in supine position with open eyes, after steady conditions were reached. All the subjects were tested twice, in identical conditions, once before and once after the exercise-training period.

■ Measurements

The ECG was recorded with a standard apparatus (OTE Biomedica, Italy), beat-to-beat blood pressure with a non-invasive finger photoplethysmograph (Finapres, Ohmeda 2300, Englewood, CO, USA) and respiratory airflow with a turbine-based spirometer connected to a mouthpiece. The accuracy of the Finapres readings was checked at the beginning of the recording sessions with a standard sphygmomanometer, and the Finapres cuff was re-positioned if a mismatch $> 5\%$ was found.

■ Signal processing

Off-line signal processing was performed to analyze the records in the time and in the frequency domain, as detailed in previous works from our laboratory [8, 19]. Briefly, beat-to-beat analysis of the stored signals provided time series of successive values of R-R interval (RR), systolic (SAP), diastolic (DAP), mean (MAP) arterial pressure and instantaneous respiratory airflow. Ectopic beats, if present, were substituted by linear interpolation of adjacent beats and significant trends were removed by subtracting from the time series the best-fitting regression line. We used an autoregressive monovariate approach [2] to estimate the power and central frequency associated to each spectral peak [22] in the RR and SAP time series. Two principal oscillations, namely the high frequency (HF) component, which is related to respiration, and the low frequency (LF) component ($0.05\text{--}0.15$ Hz) are essentially identified [14]. We reported for both parameters the low frequency powers (LF_{RR} and LF_{SAP}) and the high frequency powers (HF_{RR} and HF_{SAP}). We also performed transfer function analysis by a bivariate autoregressive model, to estimate the frequency-related squared coherence, the phase shift and the transfer function gain (TFG) between RR and SAP. Discrete values of phase shift and TFG between RR and SAP in the LF frequency region (TFG_LF) were taken at the frequency corresponding to the highest coherence value, where the estimate error is at a minimum [26]. If coherence is > 0.5 and the phase shift is negative, TFG_LF may be used as an index of baroreflex sensitivity (BRS) [8, 39]. Also the airflow records were processed for spectral and cross-spectral analysis, in order to confirm the respiratory origin of the HF components, and to exclude the event that the respiration rate approached the LF frequency.

■ Exercise training program

One-hour exercise sessions were carried out, from beginning of November to beginning of April, twice a week, for a total of 50 hours, under the supervision of an experienced physical education teacher. The training program considered both the metabolic and neuro-muscular aspects of the movement (including exercises for the development of strength, resistance, velocity, balance, joint mobility, and global and sectorial co-ordination). Table 1 shows the standard scheme of a gym lesson with estimated energy expenditure for each type of activity, as obtained from a Compendium of Physical Activities [1]. The purpose of the program was to keep a moderate level of effort; however, we could not prescribe individual workloads, because the subjects always performed group exercise. To give a hint of the individual exercise intensity, we reported in Table 2 the average resting and exercise heart rates (recorded by a Polar HR monitor) obtained from records taken after one month from the beginning of the course. Table 2 also reports the percentage of heart rate reserve, %HRR [$\text{mean activity HR} - \text{resting HR} / (\text{estimated HR max} - \text{resting HR})$], which has been shown to be an accurate index for the assessment of the energy expenditure [45]. Individual values ranged from 41.5 to 57.8 and the average %HRR was slightly less than 50, which indicates that the exercise performed can be globally classified as moderate.

Table 1 Scheme of a gym lesson: exercise examples with related METs (multiple of metabolic equivalent) estimate [1]

Time	Activity description	Exercise examples	Codes	METs
10–15 min	warm-up	walking, marching, slow running, movements of the legs	17170 17220	From 3.0 to 5.0
20–25 min	development of specific abilities	movements with or without tools, in pairs or in small groups, in standing or lying position	02030 03020 15300	From 3.5 to 5.0
10 min	games	team games, with or without a ball	12010 03015	From 4.0 to 6.0
10–15 min	cooling down	in a sitting or lying position, respiratory and stretching exercises	02100 02101	2.5

Table 2 Hint on the intensity of exercise from a training session. Heart rates of individual subjects in beats min^{-1} : average resting and exercise values; percent of HR reserve (% HRR) during exercise

Subject	Resting	Exercise	% HRR
1	78	116	49.3
2	84	109	57.8
3	66	104	45.2
4	79	122	44.1
5	74	118	50
6	90	124	50.5
7	70	116	44.5
8	69	114	41.5
9	74	112	52.5
10	70	120	43.8
11	79	117	48.6
Mean	75.7	115.6	48.0
SD	7.1	5.8	4.7

Statistical analysis

Data were reported as means \pm SEM. We tested the significance of differences between data recorded before and after training by Student's *t*-test for paired data. Since HF and LF powers have high interindividual variance and may not be normally distributed, we also performed the statistical test after logarithmic transformation of power values. We did not find any difference in the results of statistical analysis performed on transformed and untransformed data. Significance level was set at $p < 0.05$.

Results

Time domain results. All the results reported refer to supine resting conditions, as observed before and after the training program. Time-domain results of heart period and blood pressure are shown in Table 3. Exercise training significantly increased RR by 6% and HRV by 25%. Systolic and mean arterial pressure did not change while diastolic pressure decreased significantly by 6%.

Frequency domain results. Table 4 reports the results of spectral analysis of RR and SAP. After training, the LF_{RR} power increased significantly by 131% (Fig. 1a). On the other hand, the HF_{RR} power remained unchanged (Fig. 1b). The LF/HF ratio, therefore, was about doubled. LF_{SAP} increased significantly by 114% (Fig. 1c), while HF_{SAP} did not change.

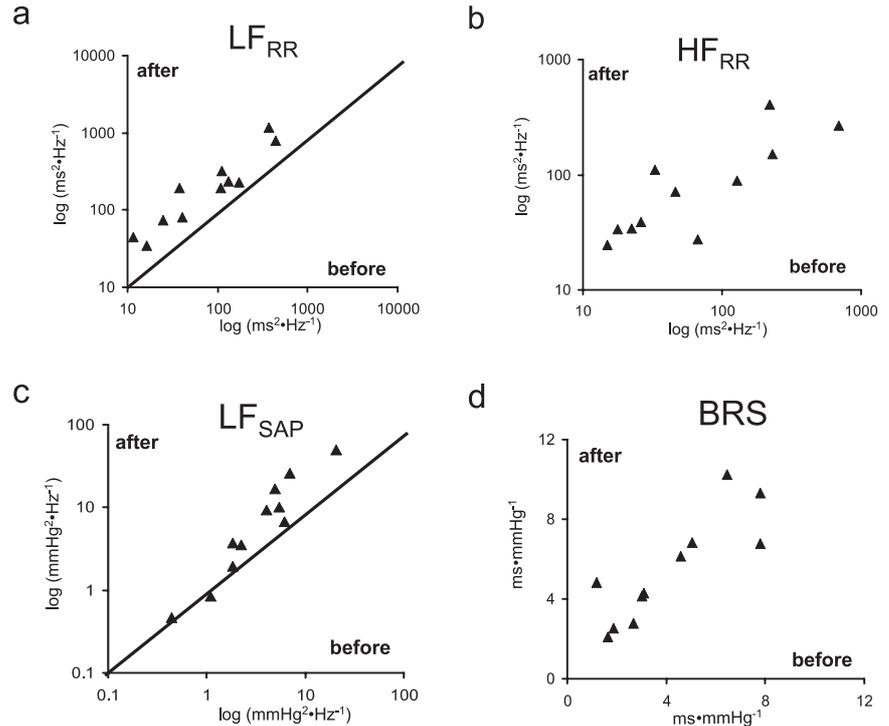
Table 4 Frequency-domain results of training in aged women. Spectral analysis of heart period (RR) and systolic arterial pressure (SAP). Mean values \pm SEM of powers in low (LF) and high (HF) frequency range before and after training. Statistical significance of changes by paired Student *t*-test

	Before	After	t-test
RR			
LF (ms^2)	133.2 \pm 43.6	307.9 \pm 107.9	$p < 0.05$
HF (ms^2)	135.7 \pm 60.2	113.9 \pm 36.6	n. s.
LF/HF	1.4 \pm 0.3	2.8 \pm 0.5	$p < 0.05$
SAP			
LF (mmHg^2)	5.0 \pm 1.7	11.8 \pm 4.4	$p < 0.05$
HF (mmHg^2)	1.4 \pm 0.4	1.6 \pm 0.4	n. s.

Table 3 Time-domain results of training in aged women. Mean value \pm SEM of heart period (RR), systolic (SAP), diastolic (DAP) and mean (MAP) arterial pressure, and their respective variance, before and after training. Statistical significance of changes by paired Student *t*-test

	RR (ms)	RR variance (ms^2)	SAP (mmHg)	SAP variance (mmHg^2)	DAP (mmHg)	DAP variance (mmHg^2)	MAP (mmHg)	MAP variance (mmHg^2)
before	894 \pm 41	868 \pm 239	137.5 \pm 5.4	28.7 \pm 6.5	75.8 \pm 3.0	5.9 \pm 1.3	97.2 \pm 3.3	10.3 \pm 2.3
after	947 \pm 31	1087 \pm 245	135.4 \pm 5.9	31.8 \pm 7.0	70.8 \pm 2.2	7.0 \pm 1.4	94.0 \pm 3.5	12.2 \pm 2.5
t-test	$P < 0.05$	$P < 0.05$	n. s.	n. s.	$P < 0.05$	n. s.	n. s.	n. s.

Fig. 1 Identity diagrams of the most important frequency-domain variables in 11 aged women before (abscissa) and after (ordinate) a 6-month aerobic training period: **a** power of low frequency oscillations of heart period (LF_{RR}), logarithmic units; **b** power of high frequency oscillations of heart period (HF_{RR}), logarithmic units; **c** power of low frequency oscillations of systolic arterial pressure (LF_{SAP}), logarithmic units; **d** transfer function gain at low frequency between RR and SAP, used as an index of baroreflex sensitivity (BRS)



The results of the cross-spectral analysis between RR and SAP fluctuations are shown in Table 5. Before training, the phase shift in the LF range was -90.6 ± 10.0 deg, indicating that RR changes lagged behind SAP changes with a delay of 1–2 heartbeats. The coherence was above 0.5 and the central frequency at the point of maximal coherence was 0.091 ± 0.006 Hz. In the respiratory range, the phase shift was near zero, indicating simultaneous changes of RR and SAP; coherence was well above 0.5 and the central frequency at the point of maximal coherence was around 0.3 Hz. After the training period, we detected, in the LF range, a significant in-

crease in coherence between SAP and RR oscillations and also a considerable increase in the BRS, by 32% (Fig. 1d). On the other hand, at the respiratory frequency we did not find significant changes in any of the cross-spectral parameters. This was also confirmed by direct measurements of the respiratory flow variability. We always detected a single respiratory peak, at 0.296 ± 0.03 Hz, and 0.289 ± 0.03 Hz, before and after the training, respectively. The power was 3.9 ± 0.05 ($l \cdot s^{-1}$)² before training and 4.0 ± 0.05 ($l \cdot s^{-1}$)² thereafter. Cross-spectral analysis did not show, in any case, a significant coherence between airflow and the other cardiovascular parameters in the LF range demonstrating that the respiratory rate did not overlap with the low frequency variability.

Table 5 Cross-spectral results of training in aged women. Mean values \pm SEM of phase, coherence and transfer function gain (TFG) between heart period and systolic arterial pressure, in the low (LF) and in the high (HF) frequency range. Statistical significance of changes by paired Student *t*-test

	Phase (degree)	Coherence	TFG (ms mmHg ⁻¹)	Frequency (Hz)
<i>LF Range</i>				
before	-90.6 ± 10.0	0.59 ± 0.03	4.1 ± 0.7	0.091 ± 0.006
after	-81.2 ± 9.3	0.66 ± 0.03	5.4 ± 0.8	0.087 ± 0.006
t-test	n. s.	$P < 0.05$	$P < 0.01$	n. s.
<i>HF Range</i>				
before	4.6 ± 11.4	0.82 ± 0.03	7.5 ± 1.4	0.278 ± 0.022
after	11.2 ± 12.3	0.78 ± 0.06	7.9 ± 1.4	0.296 ± 0.026
t-test	n. s.	n. s.	n. s.	n. s.

Discussion

The aim of this longitudinal study was to assess the effects of a moderate training program on the autonomic control of the cardiovascular system in a group of post-menopausal sedentary healthy women. We confirmed the hypothesis that a program of a specifically elderly addressed exercise training, extended over a period of six months, which was performed with large compliance by a group of older women, be adequate to induce significant changes in the autonomic function. This moderate exercise was sufficient to stop and to partially revert the decline in BRS and HRV, commonly associated

with aging and considered an important risk factor for several cardiovascular diseases [17, 31, 46].

We found an increase in the total variance of heart rate. HRV is assumed to be an index of the autonomic influence on the sinus node, especially of the parasympathetic activity [40]. Conflicting results [4, 43] on the effects of aerobic training on HRV may be attributed to the use of different methods and to the age of the subjects under study.

In other studies, where postmenopausal women were investigated, Davy et al. found enhanced HRV in well-trained postmenopausal athletes, in comparison with sedentary age-matched controls [10], while no change in HRV [11] was reported on hypertensive women after a 12-week training. The authors recognized that “constitutional makeup may have influenced *their* HRV findings independent of physical activity levels” [10] and that the exercise performed may have been not adequate to induce modifications on the autonomic function of hypertensive subjects [11]. Under this respect (HRV changes), we demonstrated that a longer and appropriate exercise program induces significant increases in normotensive postmenopausal women. However, this change in HRV was not matched with an increase in the HF oscillations. Heart period HF is almost entirely mediated by the vagal efferent activity [25] and was found to increase in very well trained subjects [18]. With our moderate exercise protocol, training failed to produce any increase in the HF oscillations of RR, despite a significant reduction in heart rate. On the contrary, it enhanced LF oscillations of RR. It must be recalled that RSA (HF_{RR}) in itself has not always been proved to be a reliable index of the total vagal traffic to the heart [28]. RSA (HF_{RR}) mostly reflects the baseline vagal tone, while the cardiac component of the baroreceptor mechanism plays an important role in the parasympathetic reflex control of heart rate [27]. Thus, the improvement of the baroreflex function we have found, rather than any increase in baseline vagal tone (HF_{RR}), might account for the bradycardia observed in our elderly subjects after physical training.

On this basis, we propose a physiological interpretation, which can provide a reasonable explanation for coexistence of bradycardia with no change in HF_{RR} and an increase in LF_{RR} variability. Although, the LF_{RR} variability has been classically interpreted mainly as a marker of the sympathetic drive to the sinus node [38], it was often suggested that LF_{RR} depends both on the sympathetic and the parasympathetic efferent controls of the heart [23]. Particularly, we [8, 19], as well as other authors [9], have proposed that, at least in the supine position, LF_{RR} variability is induced by low-frequency oscillations of peripheral resistance. These oscillations arise from the sympathetic vasomotor control, and are conveyed to the heart by the baroreflex, mainly through the efferent vagal activity. This model of the LF_{RR} origin has been re-

cently confirmed on healthy supine resting volunteers [8]. Thus, we suggest that a prolonged training program might have increased the power of LF_{RR} by enhancing the baroreflex sensitivity. We believe that also the increase in the coherence value in the LF range reflect an improvement in the baroreflex function. This consideration is supported by the consistent reduction of linearly correlated SAP-RR segments as well as of average coherence values induced by pharmacological autonomic blockade [33] and baroreceptor deafferentation in animals [34].

The issue of the effects of training on the baroreceptor reflex is controversial. The discrepancy in the results may be ascribed to the variety of the methods used and also to the age and gender of the subjects investigated [5, 10, 11, 41, 42]. In the present study, after six months of moderate training, we observed a significant increase in the BRS. This result, which differs from previous studies, probably depends on the type, rather than on the intensity, of the physical activity performed. Indeed, the exercises carried out by our subjects were principally based on a variety of different movements, rather than a repetition of the same action (as it is in walking), which induced transient changes in arterial blood pressure, requiring quick cardiovascular responses. It must be also emphasized that the method to estimate BRS in elderly by TFG_LF used in this research, was validated by James et al. [21].

The observed changes in HRV and BRS, together with bradycardia, are the most coherent findings of the present study and reflect an improved vagal control of the heart, which can play an important metabolic cardioprotective function and improve the electrical stability of the heart. However the observed increase in LF_{SAP} in the trained old women deserves a brief comment. Although LF_{SAP} is generally interpreted as an index of the vasomotor sympathetic activity, several aspects of our results, such as decrease in DAP, lack of an increase in SAP, and relative bradycardia, suggest that an increase in the sympathetic tone did not occur in our subjects after training. As an alternative explanation, we propose that exercise training produced an augmented sympathetic peripheral modulation, probably due to improved adrenergic responsiveness [44], which led to greater LF variability of blood pressure. Also an increased vascular compliance, which has been demonstrated to occur in elderly after moderate exercise [37], could be responsible not only of the improved baroreflex function [35], but also of the larger blood pressure oscillations.

Some experimental limitations of our study must be mentioned. Besides the possible role of intraindividual variability, we cannot exclude that the observed responses may be attributed, for example, to seasonal variations in the autonomic outflow [15]. If this were the case, however, we should have expected changes in the opposite direction (i. e. increase in DAP and HR, de-

crease in HRV), which have been shown to occur in the cold season [29, 47], since our training program was carried out in winter. In addition, it has been demonstrated that the BRS estimated by spectral analysis in the LF region has a good reproducibility, and is suitable for longitudinal long-term studies [12, 20].

In the present paper, we do not provide information about the effectiveness of training, such as changes in VO_{2max} or muscle strength. We recall however that our intervention was indeed not aimed at increasing strength or aerobic capacity of the subjects, but at investigating autonomic adaptations induced by a moderate group-based exercise program. Noteworthy, in a previ-

ously cited similar study by Monahan et al. [36], exercise induced an increase in BRS in older men, despite no change in aerobic capacity.

In conclusion, we emphasize that the exercise activity performed by the subjects in this research required light, relatively risk-free workloads, and included varied and enjoyable activities. This contributed to strengthen the motivation in the participants, as attested by the low dropout rate. Consequently we believe that this kind of activity, which leads to an improvement in the reflex control of the cardiovascular function and in several cardiovascular risk factors, might be suggested for the third age population.

References

- Ainsworth BE, Haskell WL, Whitt MC, et al. (2000) Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc* 32 (Suppl.):S498–S516
- Bartoli F, Baselli G, Cerutti SA (1985) R identification and spectral estimate applied to the R-R interval measurements. *Int J Bio-Medical Computing* 16:201–215
- Billman GE, Schwartz PJ, Stone HL (1982) Baroreceptor reflex control of heart rate: a predictor of sudden cardiac death. *Circulation* 66:874–879
- Boutcher SH, Stein P (1995) Association between heart rate variability and training response in sedentary middle-aged men. *Eur J Appl Physiol* 70:75–80
- Bowman AJ, Clayton RH, Murray A, et al. (1997) Effects of aerobic exercise training and yoga on the baroreflex function in healthy sedentary normotensive elderly persons. *Eur J Clin Inv* 27:443–449
- Cappelletto P, Capuzzo A, Cavallini A, et al. (1998) The influence of physical activity on aging: the “third age project” in Verona. 20th ICPAFR Symposium. In: Casagrande G, Viviani F (eds) *Physical Activity and Health: Physiological, Epidemiological and Behavioral Aspects*. Padua: Unipress, pp 207–217
- Cerati D, Schwartz PJ (1991) Single cardiac vagal fiber activity, acute myocardial ischemia, and risk for sudden death. *Circ Res* 69:1389–1401
- Cevese A, Gulli G, Polati E, et al. (2001) The baroreflex and the oscillation of heart period at 0.1 Hz studied by α -blockade and cross-spectral analysis in healthy humans. *J Physiol (Lond)* 531: 235–244
- Cooke WH, Hoag JB, Crossman AA, et al. (1999) Human responses to upright tilt: a window on central autonomic integration. *J Physiol (Lond)* 517:617–628
- Davy KP, Miniclier NL, Taylor JA, et al. (1996) Elevated heart rate variability in physically active postmenopausal women: a cardioprotective effect? *Am J Physiol* 271:H455–H460
- Davy KP, Willis WL, Seals DR (1997) Influence of exercise training on heart rate variability in post-menopausal women with elevated arterial blood pressure. *Clin Physiol* 17:31–40
- Dawson SL, Robinson TG, Youde JH, et al. (1997) The reproducibility of cardiac baroreceptor activity assessed non-invasively by spectral sequence techniques. *Clin Auton Res* 7:279–284
- Eaker ED, Chesebro JH, Sacks FM, et al. (1993) Cardiovascular disease in women. *Circulation* 88:1999–2009
- Task Force European Society of Cardiology and North American Society of Pacing and Electrophysiology (1996) Heart rate variability. (Standards of measurement, physiological interpretation and clinical use). *Circulation* 93:1043–1065
- Fagius J, Kay R (1991) Low ambient temperature increases baroreflex-governed sympathetic outflow to muscle vessels in humans. *Acta Physiol Scand* 142:201–209
- Folkow B, Svanborg A (1993) Physiology of cardiovascular aging. *Physiol Rev* 73:725–764
- Ford GA (1999) Ageing and the baroreflex. *Age Ageing* 28:337–338
- Goldsmith RL, Bigger JTJ, Steinman RC, et al. (1992) Comparison of 24 hour parasympathetic activity in endurance-trained and untrained young men. *JACC* 20:552–558
- Grasso R, Schena F, Gulli G, et al. (1997) Does low-frequency variability of heart period reflect a specific parasympathetic mechanism? *J Auton Nerv Syst* 63:30–38
- Herpin D, Ragot S (1997) Mid- and long-term reproducibility of noninvasive measurements of spontaneous arterial baroreflex sensitivity in healthy volunteers. *Am J Hypertens* 10:790–797
- James MA, Panerai RB, Potter JF (1998) Applicability of new techniques in the assessment of arterial baroreflex sensitivity in the elderly: a comparison with established pharmacological methods. *Clinical Science* 94:245–253
- Johnsen SJ, Andersen N (1978) On power estimation in maximum entropy spectral analysis. *Geophysics* 43:681–690
- Jokkel G, Bonyhay I, Kollai M (1995) Heart rate variability after complete autonomic blockade in man. *J Auton Nerv Syst* 51:85–89
- Kannel WB, Hjortland MC, McNamara PM, et al. (1976) Menopause and risk of cardiovascular disease: the Framingham study. *Ann Intern Med* 85: 447–452
- Katona PG, Jih F (1975) Respiratory sinus arrhythmia: noninvasive measure of parasympathetic cardiac control. *J Appl Physiol* 39:801–805
- Kay SM (1991) *Modern Spectral Estimation: Theory and Application*. Englewood Cliffs, New Jersey: Prentice-Hall Inc
- Kollai M, Jokkel G, Bonyhay I, et al. (1994) Relation between baroreflex sensitivity and cardiac vagal tone in humans. *Am J Physiol* 266:H21–H27
- Kollai M, Mizsei G (1990) Respiratory sinus arrhythmia is a limited measure of cardiac parasympathetic control in man. *J Physiol* 424:329–342
- Kristal-Boneh E, Froom P, Harari G, et al. (2000) Summer-winter differences in 24 h variability of heart rate. *J Cardiovasc Risk* 7:141–146

30. La Rovere MT, Bigger JT Jr, Marcus FI, et al. (1998) Baroreflex sensitivity and heart-rate variability in prediction of total cardiac mortality after myocardial infarction. ATRAMI (Autonomic Tone and Reflexes After Myocardial Infarction) Investigators [see comments]. *Lancet* 351:478–484
31. La Rovere MT, Specchia G, Mortara A, et al. (1988) Baroreflex sensitivity, clinical correlates, and cardiovascular mortality among patients with a first myocardial infarction: a prospective study. *Circulation* 78:816–824
32. Lakatta EG (1993) Cardiovascular regulatory mechanisms in advanced age. *Physiol Rev* 73:413–467
33. Legramante JM, Raimondi G, Massaro M, et al. (1999) Investigation feed-forward neural regulation of circulation from analysis of spontaneous arterial pressure and heart rate fluctuations. *Circulation* 99:1760–1766
34. Mancia G, Parati G, Castiglioni P, et al. (1999) Effect of sinoaortic denervation on frequency-domain estimates of baroreflex sensitivity in conscious cats. *Am J Physiol* 276:H1987–H1993
35. Monahan KD, Dinunno FA, Seals DR, et al. (2001) Age-associated changes in cardiovagal baroreflex sensitivity are related to central arterial compliance. *Am J Physiol Heart Circ Physiol* 281:H284–H289
36. Monahan KD, Dinunno FA, Tanaka H, et al. (2000) Regular aerobic exercise modulates age-associated declines in cardiovagal baroreflex sensitivity in healthy men. *J Physiol* 529 Pt 1: 263–271
37. Monahan KD, Tanaka H, Dinunno FA, et al. (2001) Central arterial compliance is associated with age- and habitual exercise-related differences in cardiovagal baroreflex sensitivity. *Circulation* 104:1627–1632
38. Pagani M, Lombardi F, Guzzetti S, et al. (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
39. Robbe HWJ, Mulder LJM, Ruddle H, et al. (1987) Assessment of baroreceptor reflex sensitivity by means of spectral analysis. *Hypertension* 15:538–543
40. Saul JP (1990) Beat-to-beat variations of heart rate reflect modulation of cardiac autonomic outflow. *NIPS* 5:32–37
41. Seals DR, Chase PB (1989) Influence of physical training on heart rate variability and baroreflex circulatory control. *J Appl Physiol* 66:1886–1895
42. Sheldahl LM, Ebert TJ, Cox B, et al. (1994) Effect of aerobic training on baroreflex regulation of cardiac and sympathetic function. *J Appl Physiol* 76:158–165
43. Somers VK, Conway J, Johnston J, et al. (1991) Effects of endurance training on baroreflex sensitivity and blood pressure in borderline hypertension. *Lancet* 337:1363–1368
44. Spina RJ, Bourey RE, Ogawa T, et al. (1994) Effects of exercise training on alpha-adrenergic mediated pressor responses and baroreflex function in older subjects. *J Gerontol* 49: B277–B281
45. Swain DP, Leutholtz BC, King ME, et al. (1998) Relationship between % heart rate reserve and % VO₂ reserve in treadmill exercise. *Med Sci Sports Exerc* 30:318–321
46. Tsuji H, Venditti FJ Jr, Manders ES, et al. (1994) Reduced heart rate variability and mortality risk in an elderly cohort. The Framingham Heart Study. *Circulation* 90:878–883
47. Woodhouse PR, Khaw KT, Plummer M (1993) Seasonal variation of blood pressure and its relationship to ambient temperature in an elderly population. *J Hypertens* 11:1267–1274