No Effect of Training State on Ambulatory Measures of Cardiac Autonomic Control

Annebet D. Goedhart[1], Marije de Vries[2], Jeroen Kreft[2], Frank C. Bakker[2], and Eco J.C. de Geus[1]

[1]Department of Biological Psychology, VU University Amsterdam, Amsterdam, The Netherlands,
[2]Research Institute MOVE VU University, Amsterdam, The Netherlands

Abstract. We examined the effect of training state on cardiac autonomic control in a naturalistic setting. Twenty-four vigorous exercisers were compared to age- and sex-matched sedentary controls. The regular exercisers were subjected to a 6-week training program after which they were randomized to 2 weeks of continued training or 2 weeks of detraining. Cardiac autonomic control was measured over a 24-h period by ambulatory recording, using the preejection period (PEP) and respiratory sinus arrhythmia (RSA). Nonexercising controls had a significantly higher ambulatory heart rate (HR) compared to the regular exercisers but comparable 24-h levels of PEP and RSA. In regular exercisers, 2 weeks of detraining did not significantly change the 24-h levels of HR, PEP, or RSA. We conclude that the bradycardia in healthy regular exercisers is the result of a lower intrinsic heart rate rather than a shift in cardiac autonomic balance from sympathetic to vagal control.

Keywords: exercise, detraining, heart rate, autonomic control, sympathetic, vagal

Introduction

Prospective studies have repeatedly suggested that regular vigorous exercise in leisure time (e.g., sports, jogging, aerobics) is associated with a reduced risk for myocardial infarction and sudden death (Powell, Thompson, Caspersen, & Kendrick, 1987; Williams, 2001). An exercise-induced bradycardia with a shift to less sympathetic and more parasympathetic control over the heart rhythm is one of the mechanisms put forward to explain this reduced risk in exercisers, and evidence in favor of this mechanism has accrued in animal studies and studies in cardiac patients (Billman, 2002; Goldsmith, Bloomfield, & Rosenwinkel, 2000; Gutin et al., 2005; Mueller, 2007; Rosenwinkel, Bloomfield, Arwardy, & Goldsmith, 2001). In healthy human subjects, however, the evidence for an exercise-induced shift in cardiac autonomic control is more controversial. To quantify autonomic control in exercisers and nonexercisers, various studies have used sympathetic, parasympathetic, or dual blockade. Using this pharmacological approach vagal cardiac control has sometimes been found to be higher in well-trained persons (Shi, Stevens, Foresman, Stern, & Raven, 1995; Smith, Hudson, Graitzer, & Raven, 1989), but other studies failed to find such an effect (Katona, Mclean, Dighton, & Guz, 1982; Kingwell, Dart, Jennings, & Korner, 1992). Likewise, sympathetic cardiac control was shown to be lower in exercisers than in nonexercisers in one study (Lin & Horvath, 1972), but others could not replicate this (Katona et al., 1982; Lewis, Nylander, Gad, & Areskog, 1980). In addition, regional noradrenaline (NA) spillover,direct microneurographic recordings from nerves innervating the skeletal muscle, or **[OK??]**muscle sympathetic nerve activity (MSNA) do not systematically suggest decreased sympathetic tone in exercisers (Alvarez, Halliwill, Ballard, Beske, & Davy, 2005; Meredith et al., 1991; Ray & Hume, 1998; Svedenhag, Wallin, Sundlof, & Henriksson, 1984). Taken together, studies using invasive measures of cardiac autonomic control have not found strong evidence for a favorable exercise-induced shift in sympathovagal balance. In contrast, lowered intrinsic HR in exercisers has emerged as a very consistent finding (Katona et al., 1982; Kingwell et al., 1992; Smith et al., 1989) and may be a sufficient cause for their resting bradycardia.

A disadvantage of invasive techniques (blockade, NA spillover, MSNA) is that they are confined to laboratory testing and are not readily amenable to recordings in naturalistic settings. This makes it hard to examine effects of exercise on, for instance, autonomic control at night or during job-related activities with a substantial mental and emotional load. Nonetheless, it is autonomic control during these naturalistic conditions that may have the largest clinical relevance, and understanding exercise effects on this "real life" autonomic control may be very valuable. It is further possible that more consistent effects of exercise on

autonomic cardiac control emerge in such settings. As an alternative to invasive techniques, cardiac sympathetic control can be indexed noninvasively by analyzing the preejection period (PEP), a reflection of myocardial contractility, and parasympathetic cardiac control can be indexed by time- or frequency-domain indices of heart rate variability in the respiratory frequency range, also called respiratory sinus arrhythmia (RSA).

PEP reflects β-adrenergic inotropic drive to the left ventricle as shown in laboratory studies manipulating β-adrenergic tone by epinephrine infusion (Mezzacappa, Kelsey, & Katkin, 1999; Schachinger, Weinbacher, Kiss, Ritz, & Langewitz, 2001; Svedenhag, Martinsson, Ekblom, & Hjemdahl, 1986), adrenoceptor blockade (Harris, Schoenfeld, & Weissler, 1967; Schachinger et al., 2001; Winzer et al., 1999), exercise (Krzeminski et al., 2000; Miyamoto et al., 1983; Smith et al., 1989), or emotional stress (Berntson et al., 1994; Newlin & Levenson, 1979; Sherwood, Allen, Obrist, & Langer, 1986). RSA shows virtually no sensitivity to sympathetic nervous system activity but is affected in a dose-responsive way by muscarinergic blockers in humans (Martinmaki, Rusko, Kooistra, Kettunen, & Saalasti, 2006) or vagal cooling in animals (Katona & Jih, 1975). This has led to the use of RSA as a proxy for vagal cardiac control (Berntson et al., 1997; Task Force of the European Society of Cardiology the North American Society of Pacing, 1996), with a note of caution regarding potential confounding by individual differences in sensitivity of chemoreceptor and baroreceptor reflexes (Berntson et al., 1997) and by individual differences in respiratory behavior (Grossman, Wilhelm, & Spoerle, 2004; Ritz & Dahme, 2006). Although less precise than invasive measures, the huge advantage of the PEP and RSA measures is that they can be reliably recorded in an ambulatory setting (Goedhart, Kupper, Willemsen, Boomsma, & de Geus, 2006; Goedhart, van der Sluis, Houtveen, Willemsen, & de Geus, 2007).

The link between exercise and RSA or PEP has been examined cross-sectionally by comparing highly fit vs. less fit subjects or regular exercisers vs. sedentary subjects. It has also been examined longitudinally by comparing sedentary subjects before and after a training program. Taken together, these studies suggest that highly fit regular exercisers have higher RSA than less fit nonexercisers, but that the effects of training are less convincing than cross-sectional findings (Aubert, Seps, & Beckers, 2003; Billman, 2002; Buchheit et al., 2005; de Geus et al., 1996; de Geus, van Doornen, Visser, & Orlebeke, 1990; de Meersman, 1993; Dixon, Kamath, Mccartney, & Fallen, 1992; Goldsmith, Bigger, Steinman, & Fleiss, 1992; Goldsmith, Bigger, Bloomfield, & Steinman, 1997; Hatfield et al., 1998; Kenney, 1985; Rossy & Thayer, 1998; Sacknoff, Gleim, Stachenfeld, & Coplan, 1994; Shin, Minamitani, Onishi, Yamazaki, & Lee, 1997). Neither cross-sectional nor longitudinal studies support a link between exercise and PEP (Light, Obrist, James, & Strogatz, 1987; Svedenhag et al., 1986; Svedenhag, Martinsson, Ekblom, & Hjemdahl, 1991).

Combining RSA/PEP-based studies with the invasive studies, the evidence for large shifts in autonomic control resulting from exercise is less compelling in healthy humans than it is in cardiac patients (Rosenwinkel et al., 2001) or animals (Billman & Kukielka, 2006; Mueller, 2007). It is of note, however, that most studies on the link between RSA and exercise behavior used laboratory resting conditions, whereas ambulatory recording was used in only a few studies (Goldsmith et al., 1992, 1997; Loimaala, Huikuri, Oja, Pasanen, & Vuori, 2000; Schuit et al., 1999; Stahle, Nordlander, & Bergfeldt, 1999). No studies so far have addressed the effects of exercise on ambulatory PEP levels. Based on the idea that more consistent effects of exercise on autonomic cardiac control may emerge in ambulatory settings, we here address the link between exercise and 24-h recordings of RSA and PEP. We will separate the results of nighttime and daytime recordings because previous studies have suggested that training effects on heart rate variability may be confined to the daytime but absent in the whole recording or nighttime levels (Schuit et al., 1999; Stahle et al., 1999). We also controlled for possible individual differences in posture and physical activity during the daytime, because these are known to affect PEP independently of cardiac sympathetic activity (Houtveen, Groot, & de Geus, 2005).

The current study has a cross-sectional part and an experimental longitudinal part. First, we compared ambulatory recordings of HR, PEP, and RSA in regular vigorous exercisers to age- and sex-matched sedentary subjects who had not engaged in regular exercise during the previous year. In contrast to most of the studies to date, for the experimental phase we chose a detraining paradigm. Most training studies recruit subjects who were untrained at the start of the study, and preferably have a persistent sedentary lifestyle in general, under the assumption that this will maximize training outcome. This assumption appears to have validity at face value, but ignores the possibility that sedentary subjects form a selective sample of the population who may be characterized by attenuated sensitivity to the autonomic effects of exercise. Failure to find training effects in sedentary subjects, therefore, does not preclude the possibility that such effects have occurred in moderate or vigorous exercisers. To avoid a potential selection of "autonomic nonresponders" we here deliberately chose to detrain the group of regular exercisers rather than to train the sedentary subjects. Before detraining, the exercisers were first subjected to a 6-week standardized training program to synchronize their training state, after which they were randomized to either 2 weeks of continued training or 2 weeks of detraining.

We hypothesized that exercisers would have lower ambulatory levels of HR, longer PEPs, and higher levels of RSA than nonexercisers. Two weeks of detraining were expected to lead to a decrease in ambulatory RSA and PEP, signaling decreased parasympathetic and increased sympathetic cardiac control, respectively.

Methods

Subjects

Twenty-eight regularly exercising subjects (16 males, 12 females) with a mean age of 38.0 years (*SD* = 12.2 years) were recruited from different ministries in The Hague and a police office in Amsterdam. Subjects were included only if they had been engaged in aerobic training for at least 30 consecutive minutes a day, 3 days a week for the previous year. Records of this were available because all subjects had been frequenting the same fitness center through a company-based discount program. Another 28 sex- and age-matched nonexercising subjects (16 males, mean age = 37.9, *SD* = 13.5) comprised the sedentary control group. These subjects were selected from a larger study in which they underwent a very comparable 24-h ambulatory recording session as described elsewhere (Goedhart et al., 2007). Subjects were included only if they had indicated they did not engage in regular exercise both at the time of ambulatory recording as well as in surveys collected 1 to 2 years earlier. All subjects were white-collar workers, mainly engaged in deskwork, and had no history of hypertension or cardiovascular disease.

At the start of the study, the regular exercisers were randomly divided into two groups, a continued training group and a detraining group. Both groups consisted of 13 subjects, the continued training group consisted of 8 males and 5 females and the detraining group of 7 males and 6 females. Two subjects, one male in the detraining group and one female in the continued training group, were excluded from the final analyses because of illness or failure to attend all test days. The matched controls were also excluded.

Ambulatory measurement protocols were approved by the Ethics Committee of the Vrije Universiteit; the detraining study was additionally examined by the Ethics Committee of the faculty of Human Movement Sciences. All subjects gave written consent before entering the study.

Protocol

The experimental phase encompassed a total of 8 weeks. First, both continued training and detraining groups underwent 6 weeks of supervised training. They trained on average 3.6 hours (*SD* = .9 hr) per week with a minimum of 3 times per week, for at least 1 hour at a minimal intensity of 70% of the maximal HR, measured with a Polar A5 HR monitor. Maximal HR was established during an all-out test on a bicycle ergometer (10 min warm-up at 130 bpm followed by two bouts of 60 s of bicycling at an increasing resistance until exhaustion). All exercises were done on exercising apparatus specially adapted for conditioning the cardiovascular system (bicycle ergometer, rowing ergometer, crosstrainer, treadmill). A research assistant was present during all exercise sessions to record compliance. This phase was intended to synchronize training states prior to the start of the actual detraining manipulation. In the next phase, the continued training group, acting here as the control group, continued the previous training regime for another 2 weeks, whereas the detraining group had to completely refrain from sports activities or other vigorous activities in leisure time. During the 2-week detraining period, subjects' absence in the fitness center was actively monitored and compliance was further checked by regular email. Subjects were ambulatory monitored for a 24-h period at the start (0 weeks) and end (6 weeks) of the run-in training phase and at the end of the detraining period (8 weeks). They were instructed to keep physical activity at a minimal level on the ambulatory monitoring day and all recordings took place at least 1 day after a training session.

Ambulatory Measurements

The Vrije Universiteit Ambulatory Monitoring System (VU-AMS) continuously recorded the electrocardiogram (ECG) and the impedance cardiogram (ICG) using six disposable, pregelled Ag/AgCl electrodes (de Geus, Willemsen, Klaver, & van Doornen, 1995; Riese et al., 2003; Willemsen, de Geus, Klaver, van Doornen, & Carroll, 1996). Subjects were instructed to wear the device the entire day and night until awakening the next morning. The VU-AMS produced an audible alarm approximately every 60 min (± 10 min, randomized) to prompt the subject to fill out an activity diary. They were instructed to write down their physical activity and bodily postures during the previous 60 min in chronological order. Diary prompting was disabled during sleep, but regular beat-to-beat recording of the ECG/ICG was maintained throughout the night. The following day the subjects were visited again to collect the equipment. For the exercisers enrolled in the detraining study this was repeated three times. The nonexercisers were ambulatory monitored for a single 24-h period only.

Ambulatory Signal Scoring

The three target variables were HR, PEP and RSA. Scoring of these variables is described in detail elsewhere (Goedhart et al., 2006, 2007). Briefly, from the ECG (sampling rate 1000 Hz) the HR was obtained from the time between two adjacent R waves. PEP was defined from the ECG and ICG as the time interval from the Q-wave onset, the onset of the electromechanical systole, to the B-point (from the ICG), which signals opening of the aortic valves (Sherwood et al., 1990; Willemsen et al., 1996). RSA was obtained from the ECG and respiration signals by subtracting the shortest IBI during HR acceleration in the inspirational phase from the longest IBI during deceleration in the expirational phase. When no phase-related acceleration or deceleration was found, the breath was assigned a RSA score of zero. Automatic scoring of PEP and RSA was checked by visual inspection of the impedance and respiratory signal from the entire recording.

Table 1. HR, PEP, and RSA in the nonexercisers ($N = 26$) and exercisers ($N = 24$) in each of the ambulatory conditions. The table displays the means and standard deviations

Measure	Group	Sleep	Sitting	Mild physical activity
HR (bpm)	Nonexercisers	62.4 (5.7)*	77.4 (7.1)*	88.1 (9.9)*
	Exercisers	57.6(10.8)	70.2 (11.5)	81.0 (12.3)
PEP (ms)	Nonexercisers	108.5 (16.9)	101.6 (19.4)	98.1 (17.5)
	Exercisers	110.6 (15.2)	103.0 (15.1)	98.1 (13.6)
RSA (ms)	Nonexercisers	53.6 (34.2)	42.4 (18.5)	33.8 (10.3)
	Exercisers	45.4 (19.5)	45.1 (22.7)	38.8 (19.9)

*Significant difference ($p < .05$) between the groups.

Using the activity diary entries in combination with a visual display of the output of a built-in vertical accelerometer, the entire 24-hr recording was divided into fixed periods. These periods were coded for posture (supine, sitting, standing, walking, bicycling), physical activity (e.g., desk work, dinner, meetings, watching TV), and physical load (no load, light, intermediate, heavy). Minimum duration of periods was always 5 min and maximum duration was always 1 h. If periods with similar activity and posture lasted more than 1 h (e.g., during sleep), they were divided into multiple periods of maximally 1 h. All periods were classified into three main ambulatory conditions: (1) lying asleep, (2) sitting during the day, or (3) mild physical activity (standing/walking) based on the dominant posture/activity reported in that period; the exact timing of changes in posture/activity was verified using the accelerometer signal from the ambulatory device. Average HR and PEP was determined across each of these conditions.

For RSA a slightly different approach was used, based on the observation by Goldberger, Kim, Ahmed, and Kadish (1996) that very low heart rates, e.g., those achieved in regular exercisers at night, can be accompanied by a paradoxical decrease in RSA, potentially reflecting a ceiling in the effects of acetylcholine on the pacemaker cells near the level of complete saturation of muscarinergic receptors. To deal with this we computed mean nighttime RSA using only those breaths in which the minimum heart rate was at least 45 bpm. This level was chosen as being the "safe point" from visual inspection of the raw nighttime HR-RSA scatter plots of all exercisers. At lower heart rates, the otherwise linear relationship between HR and RSA started to show a downward curve in seven of the subjects. In two of these subjects, these effects were extreme and nighttime HR almost never exceeded the critical level. This led to a severe distortion of RSA, which became lower than during daytime sitting and even mild physical activity. We, post-hoc, excluded these subjects from further analyses.

Statistical Analysis

For the cross-sectional analyses, mean HR, PEP, and RSA of the nonexercising subjects was compared to the mean values on the first measurement in the regular exercisers using a repeated measures ANOVA with group (nonexercisers, exercisers) as a between-subject factor and ambulatory condition (sleep, sitting, mild physical activity) as a within-subject factor. For the longitudinal analyses, a single omnibus repeated measures ANOVA with Group (continued training, detraining) as a between-subject factor and Time (0 weeks, 6 weeks, 8 weeks) and Ambulatory Condition (sleep, sitting, mild physical activity) as within-subject factors were used. To establish that the groups had comparable levels of HR, PEP, and RSA after the run-in 6-weeks standardized training program, we tested the Group by Condition effect at the start of the detraining phase (after 6 weeks). To test for an effect of detraining we examined the interactions of Group (continued training, detraining) by Time (6 weeks, 8 weeks) and Group (continued training, detraining) by Time (6 weeks, 8 weeks) by Ambulatory Condition (sleep, sitting, mild physical activity). The Greenhouse-Geisser epsilon (ε) was reported when the sphericity assumption was violated (i.e., if the Mauchly test of sphericity was statistically significant at $p < .05$) and partial η^2 (η_p^2) was reported as a measure of effect size. Because the RSA distributions were skewed, its natural logarithm was used in all further analyses.

Results

Cross-Sectional Comparison

Table 1 presents means and standard deviations for HR, PEP, and RSA separately for the nonexercisers and exercisers.

The repeated measures ANOVA showed significant main effects of posture on HR, $F(2, 49) = 190.37$, $\varepsilon = 0.72$, corrected $p = .00$, $\eta_p^2 = .86$, PEP, $F(2, 49) = 46.36$, $\varepsilon = 0.58$, corrected $p = .00$, $\eta_p^2 = .40$, and RSA, $F(2, 47) = 22.74$, $\varepsilon = 0.69$, corrected $p = .00$, $\eta_p^2 = .35$. The HR increased significantly from sleep to sitting to mild physical activity. In parallel, we found a significant linear decrease in PEP, from sleep to sitting to mild physical activity. RSA was significantly lower during mild physical activity compared to lying asleep and daytime sitting. These patterns are compatible with the expected increase in sympathetic and decrease in parasympathetic cardiac control when go-

Table 2. HR, PEP, and RSA in the continued training (N = 13) and detraining (N = 11) groups per time point and for the different ambulatory conditions. The table displays the means and standard deviations

Measure	Group	Time	Phase	Sleep	Sitting	Mild physical activity
HR (bpm)	Continued training	0 weeks	Start of training	58.5 (10.2)	71.3 (9.3)	81.5 (8.4)
	detraining			56.7 (11.7)	69.2 (13.7)	80.6 (15.7)
	continued training	6 weeks	Start of detraining	56.5 (10.1)	69.3 (8.5)	78.2 (7.9)[a]
	detraining			56.5 (12.4)	70.4 (13.6)	80.3 (12.1)
	continued training	8 weeks	End of detraining	57.1 (10.7)[b]	72.4 (12.0)	83.4 (11.3)
	detraining			56.1 (9.7)	70.6 (10.3)	79.6 (9.7)
PEP (ms)	Continued training	0 weeks	Start of training	106.7 (16.3)	100.1 (16.1)	95.9 (14.2)
	detraining			114.5 (13.6)	105.8 (14.0)	100.4 (13.1)
	Continued training	6 weeks	Start of detraining	114.7 (12.4)	102.9 (10.1)	98.8 (8.6)[a]
	Detraining			116.2 (13.4)	105.0 (13.1)	100.2 (10.8)
	Continued training	8 weeks	End of detraining	115.2 (13.3)[b]	105.5 (10.7)	99.8 (10.9)
	Detraining			119.7 (11.8)	107.5 (11.5)	102.4 (9.8)
RSA (ms)	Continued training	0 weeks	Start of training	49.1 (22.7)	44.69 (20.9)	38.8 (19.9)
	Detraining			39.9 (17.7)[c]	38.8 (20.7)	33.8 (17.8)
	Continued training	6 weeks	Start of detraining	48.1 (17.7)	43.0 (17.0)	37.9 (15.2)[a]
	Detraining			45.1 (22.8)	41.7 (21.5)	34.2 (19.2)
	Continued training	8 weeks	End of detraining	52.5 (23.0)[b]	41.6 (22.0)	32.9 (17.3)
	Detraining			42.0 (17.2)	39.7 (18.4)	31.7 (15.4)

[a]N = 12, [b]N = 11, [c]N = 10.

ing from sleep to (active) daytime activities (Burgess, Trinder, Kim, & Luke, 1997).

A significant effect involving group (nonexercisers, exercisers) was found for HR, $F(1, 50) = 6.5$, $p = .01$, $\eta_p^2 = .12$. There was no interaction with ambulatory condition and posthoc testing confirmed that exercisers had a significantly lower HR at sleep (57.6 vs. 62.4), during sitting (70.2 vs. 77.4), as well as during mild physical activity (81.0 vs. 88.1). No significant main effects of group were found for PEP and RSA and no interaction effects were found between group and ambulatory condition.

Detraining Effects

Data for the continued training and detraining groups are presented in Table 2 for each time point and for the different ambulatory conditions. At the beginning of the detraining manipulation, after the 6 weeks standardized training program, no significant differences in HR, PEP, or RSA were found between the continued training and detraining groups in any of the ambulatory conditions. More importantly, repeated measures analyses across the 2 weeks continued training/detraining period showed no Group by Time (overall ambulatory level) or Group by Time by Ambulatory Condition interaction for HR, PEP, or RSA. This is depicted in Figure 1, which shows the group differences at the beginning and end of the detraining manipulation in the three ambulatory conditions. The 2 weeks of continued training vs. 2 weeks of detraining did not induce the hypothesized decreases in PEP or RSA that would have been compatible with a shift from vagal to sympathetic cardiac control.

Because large individual differences may exist in the response to training, it is possible that strong autonomic effects in a few subjects were drowned out by smaller effects in the majority of subjects. To examine this, Figure 2 plots the 2-week changes in PEP and RSA for all subjects during sitting activities. Although a few subjects showed substantial inverse changes in PEP and RSA over the 2-week period, this occurred in detraining and continued training groups alike. This argues in favor of random variation in these parameters rather than a systematic de-training effect.

Discussion

This study examined the effect of training state on cardiac autonomic control in a naturalistic setting using PEP and RSA as proxy measures for sympathovagal balance. A cross-sectional comparison of subjects who had been engaged in regular vigorous exercise with persistent sedentary subjects revealed no differences in PEP and RSA throughout a 24-hour recording period, although HR was substantially lower at all time points.

Previous studies on the link between exercise and RSA have focused mainly on short-term laboratory recordings. A number of these studies reported higher RSA in regular vigorous exercisers (Buchheit et al., 2005; Dixon et al., 1992; Goldsmith et al., 1992; Shin et al., 1997) but not all

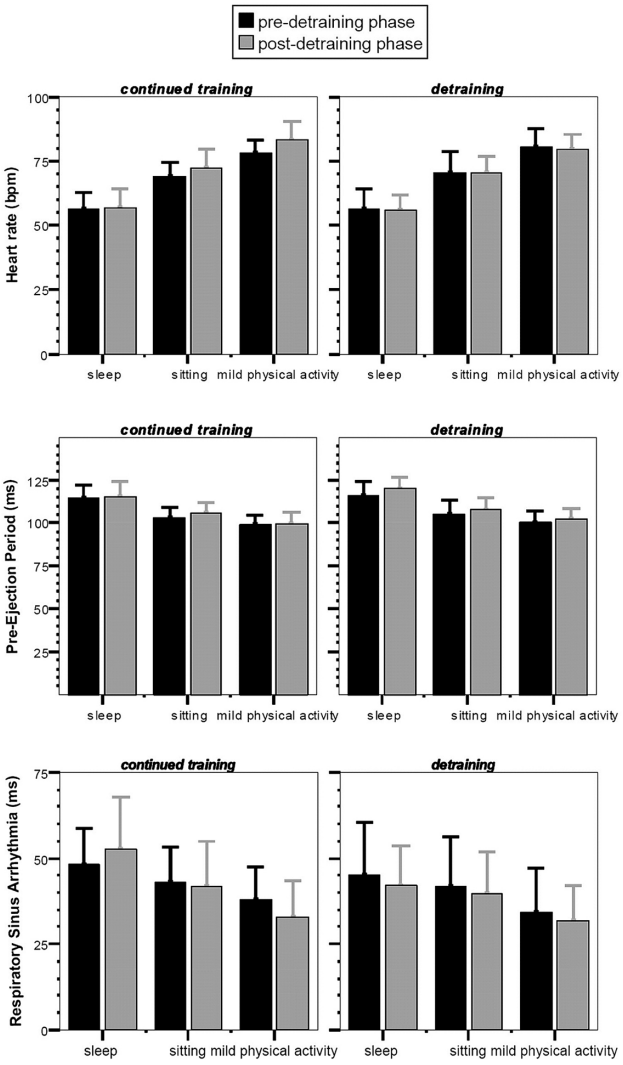

Figure 1. Bar graphs of the mean heart rate, preejection period and respiratory sinus arrhythmia per ambulatory condition before and after the detraining phase separately for the continued training and detraining group.

studies support this cross-sectional difference (Hatfield et al., 1998) and some even report the opposite finding of lower RSA in exercisers compared to nonexercisers (Sacknoff et al., 1994). Studies assessing aerobic fitness rather than exercise status have reported higher RSA in the more aerobically fit subjects (Kenney, 1985; Rossy & Thayer, 1998), even in an ambulatory setting (Goldsmith et al., 1997), but the correlation is not always found (de Geus et al., 1996, 1990; Hatfield et al., 1998). To date, a much smaller number of studies had examined the cross-sectional link between exercise and PEP. Only one study has found longer PEPs, signaling decreased sympathetic cardiac control, in exercisers compared to nonexercisers during baseline resting conditions (van Doornen & de Geus, 1989). Others have not found such an effect (Light et al., 1987; Svedenhag et al., 1986, 1991).

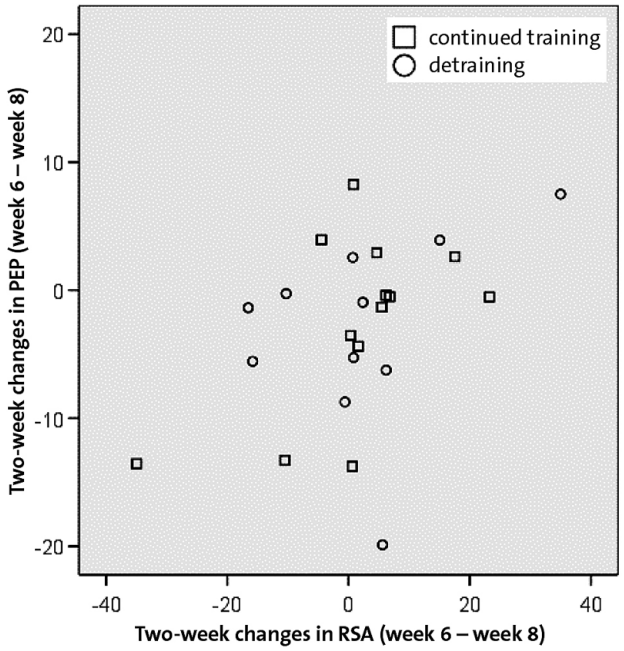

Figure 2. Correlation between the two–week changes in PEP (ms) and RSA (ms) during sitting activities in the continued training (open squares, $r = .57$) and detraining (open circles, $r = .33$) groups.

Cross-sectional comparisons suffer from the short-coming that they may be confounded by the effects of unmeasured "third variables" like genetics or socioeconomic factors. These may either create spurious associations between fitness or exercise behavior and autonomic nervous system activity (Hautala et al., 2003), or act to hide a true association. To establish causality, a number of longitudinal training studies have been performed that have been reviewed by Sandercock, Bromley, and Brodie (2005). Meta-analysis suggested an average increase in RSA during short-term laboratory recordings at rest but not in ambulatory recordings. From their Figure 2, this meta-analytic result appears to be largely driven by two studies that did not include a comparison control group (Carter, Banister, & Blaber, 2003; Iwasaki, Zhang, Zuckerman, & Levine, 2003), which makes it hard to separate effects of habituation to the measurement procedures from training effects. The training studies that (randomly) assigned untrained subjects to a nonexercise control manipulation or a standardized exercise training program have generally failed to find a specific training-induced increase in RSA (Boutcher & Stein, 1995; de Geus et al., 1996, 1990; Loimaala et al., 2000; Uusitalo, Tahvanainen, Uusitalo, & Rusko, 2004**[not in refs or 1996?]**). All training studies that added PEP as a measure have failed to find changes in PEP, even after prolonged exercise training (de Geus, van Doornen, & Orlebecke, 1993, de Gues et al., 1990; Sherwood, Light, & Blumenthal, 1989; Svedenhag et al., 1986, 1991).

Although more powerful than cross-sectional studies,

training studies also have specific shortcomings. By necessity, training studies have to select subjects who were untrained at the start of the study and who, preferably, had a sedentary lifestyle in general. In view of the emerging evidence that there are strong genetic differences in the response to training parameters like maximal oxygen uptake ($VO_{2\,max;}$ Bouchard & Rankinen, 2001) and HR (Rice et al., 2002), sedentary subjects may potentially represent a selected group of autonomic low or nonresponders. Low exercise responsiveness may even contribute to sedentary behavior if the same genetic factor that prevents large shifts in autonomic cardiac control also decreases the propensity to engage in regular exercise behavior. Evidence in favor of such an underlying factor was provided by a twin study that showed a significant genetic correlation between RSA and weekly energy expenditure in leisure time exercise (de Geus et al., 1993). To avoid a potential selection of "autonomic nonresponders" while still addressing causality, the current study examined the effects of 2 weeks of detraining on the cardiac autonomic control of regular exercisers, who had been standardized in their training practices in the preceding 6 weeks.

In contrast to our hypothesis, no significant effects of 2 weeks of detraining were found on PEP, an index of sympathetic cardiac control, or on RSA, an index of parasympathetic cardiac control. Detraining effects were absent throughout the 24-hour recording. i.e., during sleep, during sitting daytime activities, as well as during mild physical activity. Our results are in keeping with findings by Weinstein, Deuster, and Kop (2007), who used a similar design in which regular exercisers were randomized to continued training or 2 weeks of exercise deprivation. Subjects in neither control nor exercise-withdrawal groups showed alterations in RSA during 10 min of quiet sitting. Exercise-withdrawal also failed to show an effect on resting levels of low frequency heart-rate variability (LF), a measure that has been used as an alternative to PEP to index cardiac sympathetic control.

Detraining findings obtained in regular exercisers seem to differ somewhat from the findings in recently trained subjects. Pichot et al. (2002) trained six sedentary subjects for 13 weeks followed by 7 weeks of recovery. Using nighttime levels, a significant drop in the ratio of LF/HF was found during training, which was interpreted as a shift toward more vagal control over the heart. Seven weeks of detraining did not reverse this shift in LF/HF ratio. De Geus et al (1993, 1996) subjected 12 sedentary subjects to 4 months of training followed by 4 months of detraining and compared these to a nontraining control group. Although HR significantly decreased with training and fully returned to baseline levels after detraining, no parallel changes in PEP or RSA were found. Gamelin, Berthoin, Sayah, Libersa, & Bosquet (2007) trained 10 sedentary subjects for 12 weeks followed by 8 weeks of training cessation. Training significantly increased supine LF and tended to increase supine HF, leaving the LF/HF ratio unchanged. The increase in LF was reversed by 2 weeks of detraining. No effects of training or detraining were found on LF or HF at 60° tilt. Finally, Gutin et al. (2000) followed 70 obese 7- to 11-year-old children for 8 months in a randomized crossover design. Half of the children first trained for 4 months and then detrained for 4 months; the other half acted as a waiting-list control for 4 months followed by 4 months of training. Their index of parasympathetic control, the **[please define]**RMSSD, closely followed the training manipulation such that training increased RMSSD by about 6 ms, whereas detraining completely reversed this effect.

With the exception of the obese children, the current evidence does not make a compelling case in favor of short-term shifts from sympathetic to parasympathetic cardiac control, either in regular exercisers or recently trained subjects. Perhaps such training effects are confined to populations characterized by high levels of sympathetic control and low levels of parasympathetic control. Evidence in favor of this idea comes from a study by Roveda and colleagues (2003), who subjected heart failure patients and healthy controls to a supervised 4-month exercise program. At the start of the exercise program, heart failure patients had significantly higher MSNA than age-matched healthy controls. After 4 months of exercise, MSNA in the heart failure patients showed a significant decrease to the level of the healthy controls, whereas MSNA levels in the healthy controls were not influenced by the exercise program at all.

The idea that exercisers differ from nonexercisers in sympathovagal balance is primarily driven by their lower resting HR, a systematic finding across many studies that was reconfirmed in the current study. The exercise bradycardia is robust to correction for genetic influences and seems to reflect a true causal effect of exercise (de Geus et al., 2003). Training of previously sedentary subjects often leads to a decrease in HR (reviewed in: Fagard & Cornelissen, 2007) and even short periods of detraining can decrease HR to untrained levels in subjects who were only recently trained (Mujika & Padilla, 2000; Wang, Jen, & Chen, 1997). A different picture emerges for subjects who have been involved in regular exercise for many years, like the regular exercisers participating in this study. No effects of detraining were noticeable on either basal HR at sleep or HR during the daytime. These findings are in keeping with other studies that found that detraining that lasts 2 to 4 weeks did not result in a change in resting HR in highly trained athletes or in regularly trained individuals (Cullinane, Sady, Vadeboncoeur, Burke, & Thompson, 1986; Mujika & Padilla, 2000; Weinstein et al., 2007). Longer term detraining in these subjects, however, does seem to reverse bradycardia not only in recently trained subjects but also in well-trained athletes (Bonaduce et al., 1998; de Geus et al., 1996; Mujika & Padilla, 2001)

We believe that an exercise-induced decrease in intrinsic HR provides a parsimonious explanation for the paradoxical absence of clear-cut effects of training and detraining on sympathovagal balance paired to the strong evidence for exercise-induced bradycardia (Bonaduce et

al., 1998; de Geus et al., 1996). Dual-blockade studies indeed point to a lower intrinsic HR as the most replicated source of resting bradycardia in exercisers (Katona et al., 1982; Kingwell et al., 1992; Lewis et al., 1980; Smith et al., 1989; Uusitalo et al., 1996) and this is supported by findings in animals (Lin & Horvath, 1972; Negrao, Moreira, Brum, Denadai, & Krieger, 1992). Although the exact physiological mechanism causing a reduction in intrinsic HR remains elusive, it has been hypothesized that it may be caused by a mechanical effect on the pacemaker tissue imposed by cardiac hypertrophy or by an alteration in myocardial cell metabolism (Bhan & Scheuer, 1972; Katona et al., 1982). The combined results from detraining studies suggest that these adaptations apparently take time, but once in place are robust against short periods of detraining but ultimately reversible by longer periods of detraining (Mujika & Padilla, 2001).

There are some limitations of the present study that should be discussed. First, our sample size was adequate only to detect moderate to large changes in autonomic control in the 2-week period but would have missed small effects. This is aggravated by the short detraining period used, which may be too short to undo the autonomic effects for subjects who had regularly exercised for years or even decades. Also, sample size did not allow us to test detraining effects in subgroups, whereas age, gender, and aerobic fitness level may all be important moderators of training and detraining effects.

Second, we did not verify the detraining manipulation by maximal performance tests or $VO_{2\,max}$ recording. We, instead, ensured compliance by making the importance of adhering to the study design very clear at enrollment. The participants, high-level executives in the ministry or the police office, are characterized by high conscientiousness. Because they were recruited in the office-based fitness center, they were well known there, creating a strong level of social control. In addition, there was active surveillance of the fitness center itself by research assistants throughout the study. Finally, the exit interview, which recorded their physical activity over the previous 2 weeks, suggested that they had not engaged in compensatory physical activity otherwise (gardening, extra commuter bicycling etc).

Third, the PEP and RSA measures that were used to index cardiac autonomic control may be imperfect measures of vagal and sympathetic cardiac control in training/detraining studies. Changes in end-diastolic filling and mean arterial pressure can affect PEP without true changes in sympathetic cardiac control and changes in respiratory rate or depth may influence RSA independent of changes in parasympathetic control (Grossman et al., 2004). Although we did not find evidence for detraining effects on respiration rate and impedance-derived stroke volume (data not shown) no recording of blood pressure or tidal volume was done. Hence, we cannot rule out detraining effects on these measures, which might compromise the interpretation of PEP and RSA.

Conclusion

This study shows that regular exercise is not associated with changes in nighttime or daytime levels of PEP or RSA and that 2 weeks of training cessation in regular exercisers does not change their ambulatory PEP or RSA levels. This study is the first study to address the effects of training state and detraining on these measures using prolonged ambulatory recording rather than short-term laboratory testing. In spite of study limitations, the results correspond to those obtained in previous training and detraining studies using PEP, the LF/HF ratio, RSA, or more invasive indices of autonomic control, although there are clear exceptions (Gutin et al. 2000; Gamelin et al. 2007). We conclude that, in healthy subject populations, changes in ambulatory heart rate induced by training and detraining may be explained, to a large extent, by changes in intrinsic heart rate. The exact role of additional shifts in cardiac autonomic control remains to be established.

References

Alvarez, G.E., Halliwill, J.R., Ballard, T.P., Beske, S.D., & Davy, K.P. (2005). Sympathetic neural regulation in endurance-trained humans: Fitness vs. fatness. *Journal of Applied Physiology, 98,* 498–502.

Aubert, A.E., Seps, B., & Beckers, F. (2003). Heart rate variability in athletes. *Sports Medicine, 33,* 889–919.

Berntson, G.G., Bigger, J.T., Jr., Eckberg, D.L., Grossman, P., Kaufmann, P.G., Malik, M. et al. (1997). Heart rate variability: Origins, methods, and interpretive caveats. *Psychophysiology, 34,* 623–648.

Berntson, G.G., Cacioppo, J.T., Binkley, P.F., Uchino, B.N., Quigley, K.S., & Fieldstone, A. (1994). Autonomic cardiac control. III. Psychological stress and cardiac response in autonomic space as revealed by pharmacological blockades. *Psychophysiology, 31,* 599–608.

Bhan, A.K., & Scheuer, J. (1972). Effects of physical training on cardiac actomyosin adenosine triphosphatase activity. *The American Journal of Physiology, 223,* 1486–1490.

Billman, G.E. (2002). Aerobic exercise conditioning: A nonpharmacological antiarrhythmic intervention. *Journal of Applied Physiology, 92,* 446–454.

Billman, G.E., & Kukielka, M. (2006). Effects of endurance exercise training on heart rate variability and susceptibility to sudden cardiac death: Protection is not due to enhanced cardiac vagal regulation. *Journal of Applied Physiology, 100,* 896–906.

Bonaduce, D., Petretta, M., Cavallaro, V., Apicella, C., Ianniciello, A., Romano, M., et al. (1998). Intensive training and cardiac autonomic control in high level athletes. *Medicine and Science in Sports and Exercise, 30,* 691–696.

Bouchard, C., & Rankinen, T. (2001). Individual differences in response to regular physical activity. *Medicine and Science in Sports and Exercise, 33,* S446–S451.

Boutcher, S.H., & Stein, P. (1995). Association between heart rate variability and training response in sedentary middle-aged

men. *European Journal of Applied Physiology and Occupational Physiology, 70,* 75–80.

Buchheit, M., Simon, C., Charloux, A., Doutreleau, S., Piquard, F., & Brandenberger, G. (2005). Heart rate variability and intensity of habitual physical activity in middle-aged persons. *Medicine and Science in Sports and Exercise, 37*, 1530–1534.

Burgess, H.J., Trinder, J., Kim, Y., & Luke, D. (1997). Sleep and circadian influences on cardiac autonomic nervous system activity. *AJP – Heart and Circulatory Physiology, 273*, 1761–1768.

Carter, J.B., Banister, E.W., & Blaber, A.P. (2003). Effect of endurance exercise on autonomic control of heart rate. *Sports Medicine, 33*, 33–46.

Cullinane, E.M., Sady, S.P., Vadeboncoeur, L., Burke, M., & Thompson, P.D. (1986). Cardiac size and VO2Max do not decrease after short-term exercise cessation. *Medicine and Science in Sports and Exercise, 18*, 420–424.

de Geus, E.J., van Doornen, L.J., & Orlebeke, J.F. (1993). Regular exercise and aerobic fitness in relation to psychological make-up and physiological stress reactivity. *Psychosomatic Medicine, 55*, 347–363.

de Geus, E.J., Willemsen, G.H., Klaver, C.H., & van Doornen, L.J. (1995). Ambulatory measurement of respiratory sinus arrhythmia and respiration rate. *Biological Psychology, 41*, 205–227.

de Geus, E.J.C., Karsdorp, R., Boer, B., de Regt, G., Orlebeke, J.F., & van Doornen, L.J.P. (1996). Effect of aerobic fitness training on heart rate variability and cardiac baroreflex sensitivity. *Homeostasis, 37*, 28–51.

[not cited in text]de Geus, E.J.C., Boomsma, D.I., & Snieder, H. (2003). Genetic correlation of exercise with heart rate and respiratory sinus arrhythmia. *Medicine and Science in Sports and Exercise, 35*, 1287–1295.

de Geus, E.J.C., van Doornen, L.J.P., Visser, D.C., & Orlebeke, J.F. (1990). Existing and training induced differences in aerobic fitness, their relationship to physiological response patterns during different types of stress. *Psychophysiology, 27*, 457–477.

de Meersman, R.E. (1993). Heart rate variability and aerobic fitness. *American Heart Journal, 125*, 726–731.

Dixon, E.M., Kamath, M.V., Mccartney, N., & Fallen, E.L. (1992). Neural regulation of heart rate variability in endurance athletes and sedentary controls. *Cardiovascular Research, 26*, 713–719.

Fagard, R.H., & Cornelissen, V.A. (2007). Effect of exercise on blood pressure control in hypertensive patients. *European Journal of Cardiovascular Prevention and Rehabilitation, 14*, 12–17.

Gamelin, F.X., Berthoin, S., Sayah, H., Libersa, C., & Bosquet, L. (2007). Effect of training and detraining on heart rate variability in healthy young men. *International Journal of Sports Medicine,* 564–570.

Goedhart, A.D., Kupper, N., Willemsen, G., Boomsma, D.I., & de Geus, E.J.C. (2006). Temporal stability of ambulatory stroke volume and cardiac output measured by impedance cardiography. *Biological Psychology, 72*, 110–117.

Goedhart, A.D., van der Sluis, S., Houtveen, J.H., Willemsen, G., & de Geus, E.J.C. (2007). Comparison of time and frequency domain measures of RSA in ambulatory recordings. *Psychophysiology, 44*, 203–215.

Goldberger, J.J., Kim, Y.H., Ahmed, M.W., & Kadish, A.H. (1996). Effect of graded increases in parasympathetic tone on heart rate variability. *Journal of Cardiovascular Electrophysiology, 7*, 594–602.

Goldsmith, R.L., Bigger, J.T., Bloomfield, D.M., & Steinman, R.C. (1997). Physical fitness as a determinant of vagal modulation. *Medicine and Science in Sports and Exercise, 29*, 812–817.

Goldsmith, R.L., Bigger, J.T., Steinman, R.C., & Fleiss, J.L. (1992). Comparison of 24-hour parasympathetic activity in endurance-trained and untrained young men. *Journal of the American College of Cardiology, 20*, 552–558.

Goldsmith, R.L., Bloomfield, D.M., & Rosenwinkel, E.T. (2000). Exercise and autonomic function. *Coronary Artery Disease, 11*, 129–135.

Grossman, P., Wilhelm, F.H., & Spoerle, M. (2004). Respiratory sinus arrhythmia, cardiac vagal control, and daily activity. *AJP – Heart and Circulatory Physiology, 287*, H728–H734.

Gutin, B., Barbeau, P., Litaker, M.S., Ferguson, M., & Owens, S. (2000). Heart rate variability in obese children, relations to total body and visceral adiposity, and changes with physical training and detraining. *Obesity Research, 8*, 12–19.

Gutin, B., Howe, C.A., Johnson, M.H., Humphries, M.C., Snieder, H., & Barbeau, P. (2005). Heart rate variability in adolescents, relations to physical activity, fitness, and adiposity. *Medicine and Science in Sports and Exercise, 37*, 1856–1863.

Harris, W.S., Schoenfeld, C.D., & Weissler, A.M. (1967). Effects of adrenergic receptor activation and blockade on the systolic preejection period, heart rate, and arterial pressure in man. *J.Clin Invest**[full name please]**, 46*, 1704–1714.

Hatfield, B.D., Spalding, T.W., Santa Maria, D.L., Porges, S.W., Potts, J.T., Byrne, E.A., et al. (1998). Respiratory sinus arrhythmia during exercise in aerobically trained and untrained men. *Medicine and Science in Sports and Exercise, 30*, 206–214.

Hautala, A.J., Makikallio, T.H., Kiviniemi, A., Laukkanen, R.T., Nissila, S., Huikuri, H.V., et al. (2003). Cardiovascular autonomic function correlates with the response to aerobic training in healthy sedentary subjects. *American Journal of Physiology-Heart and Circulatory Physiology, 285*, H1747–H1752.

Houtveen, J.H., Groot, P.F.C., & de Geus, E.J.C. (2005). Effects of variation in posture and respiration on RSA and preejection period. *Psychophysiology, 42*, 713–719.

Iwasaki, K.I., Zhang, R., Zuckerman, J.H., & Levine, B.D. (2003). Dose-response relationship of the cardiovascular adaptation to endurance training in healthy adults, how much training for what benefit? *Journal of Applied Physiology, 95*, 1575–1583.

Katona, P.G., & Jih, F. (1975). Respiratory sinus arrhythmia, noninvasive measure of parasympathetic cardiac control. *Journal of Applied Physiology, 39*, 801–805.

Katona, P.G., Mclean, M., Dighton, D.H., & Guz, A. (1982). Sympathetic and parasympathetic cardiac control in athletes and nonathletes at rest. *Journal of Applied Physiology, 52*, 1652–1657.

Kenney, W.L. (1985). Parasympathetic control of resting heart-rate – Relationship to aerobic power. *Medicine and Science in Sports and Exercise, 17*, 451–455.

Kingwell, B.A., Dart, A.M., Jennings, G.L., & Korner, P.I. (1992). Exercise training reduces the sympathetic component of the blood-pressure heart-rate baroreflex in man. *Clinical Science, 82*, 357–362.

Krzeminski, K., Kruk, B., Nazar, K., Ziemba, A.W., Cybulski, G., & Niewiadomski, W. (2000). Cardiovascular, metabolic, and plasma catecholamine responses to passive and active exercises. *J.Physiol Pharmacol.**[full name please]**, 51*, 267–278.

Lewis, S.F., Nylander, E., Gad, P., & Areskog, N.H. (1980). Non-autonomic component in bradycardia of endurance trained men at rest and during exercise. *Acta Physiologica Scandinavica, 109*, 297–305.

Light, K.C., Obrist, P.A., James, S.A., & Strogatz, D.S. (1987). Cardiovascular responses to stress, 2. Relationships to aerobic exercise patterns. *Psychophysiology, 24*, 79–86.

Lin, Y.C., & Horvath, S.M. (1972). Autonomic nervous control of cardiac frequency in exercise-trained rat. *Journal of Applied Physiology, 33*, 796–***[number missing]***.

Loimaala, A., Huikuri, H., Oja, P., Pasanen, M., & Vuori, I. (2000). Controlled 5-month aerobic training improves heart rate but not heart rate variability or baroreflex sensitivity. *Journal of Applied Physiology, 89*, 1825–1829.

Martinmaki, K., Rusko, H., Kooistra, L., Kettunen, J., & Saalasti, S. (2006). Intraindividual validation of heart rate variability indexes to measure vagal effects on hearts. *AJP – Heart and Circulatory Physiology, 290*, H640–H647.

Meredith, I.T., Friberg, P., Jennings, G.L., Dewar, E.M., Fazio, V.A., Lambert, G.W., et al. (1991). Exercise training lowers resting renal but not cardiac sympathetic activity in humans. *Hypertension, 18*, 575–582.

Mezzacappa, E.S., Kelsey, R.M., & Katkin, E.S. (1999). The effects of epinephrine administration on impedance cardiographic measures of cardiovascular function. *International Journal of Psychophysiology, 31*, 189–196.

Miyamoto, Y., Higuchi, J., Abe, Y., Hiura, T., Nakazono, Y., & Mikami, T. (1983). Dynamics of cardiac output and systolic time intervals in supine and upright exercise. *Journal of Applied Physiology, 55*, 1674–1681.

Mueller, P.J. (2007). Exercise training and sympathetic nervous system activity, Evidence for physical activity dependent neural plasticity. *Clinical and Experimental Pharmacology and Physiology, 34*, 377–384.

Mujika, I., & Padilla, S. (2000). Detraining, loss of training-induced physiological and performance adaptations. Part I: Short term insufficient training stimulus. *Sports Medicine, 30*, 79–87.

Mujika, I., & Padilla, S. (2001). Cardiorespiratory and metabolic characteristics of detraining in humans. *Medicine and Science in Sports and Exercise, 33*, 413–421.

Negrao, C.E., Moreira, E.D., Brum, P.C., Denadai, M.L.D.R., & Krieger, E.M. (1992). Vagal and sympathetic control of heart-rate during exercise by sedentary and exercise-trained rats. *Brazilian Journal of Medical and Biological Research, 25*, 1045–1052.

Newlin, D.B., & Levenson, R.W. (1979). Preejection period: Measuring beta-adrenergic influences upon the heart. *Psychophysiology, 16*, 546–553.

Pichot, V., Busso, T., Roche, F., Garet, M., Costes, F., Duverney, D., et al. (2002). Autonomic adaptations to intensive and overload training periods: A laboratory study. *Medicine and Science in Sports and Exercise, 34*, 1660–1666.

Powell, K.E., Thompson, P.D., Caspersen, C.J., & Kendrick, J.S. (1987). Physical activity and the incidence of coronary heart disease. *Annual Review of Public Health, 8*, 253–287.

Ray, C.A., & Hume, K.M. (1998). Sympathetic neural adaptations to exercise training in humans: Insights from microneurography. *Medicine and Science in Sports and Exercise, 30*, 387–391.

Rice, T., An, P., Gagnon, J., Leon, A.S., Skinner, J.S., Wilmore, J.H., et al. (2002). Heritability of HR and BP response to exercise training in the HERITAGE family study. *Medicine and Science in Sports and Exercise, 34*, 972–979.

Riese, H., Groot, P.F., van den Berg, M., Kupper, N.H., Magnee, E.H., Rohaan, E.J., et al. (2003). Large-scale ensemble averaging of ambulatory impedance cardiograms. *Behav.Res.Methods Instrum.Comput.****[full name please]****, 35*, 467–477.

Ritz, T., & Dahme, B. (2006). Implementation and interpretation of respiratory sinus arrhythmia measures in psychosomatic medicine: Practice against better evidence? *Psychosomatic Medicine, 68*, 617–627.

Rosenwinkel, E.T., Bloomfield, D.M., Arwardy, M.A., & Goldsmith, R.L. (2001). Exercise and autonomic function in health and cardiovascular disease. *Cardiology Clinics, 19*, 369–387.

Rossy, L.A., & Thayer, J.F. (1998). Fitness and gender-related differences in heart period variability. *Psychosomatic Medicine, 60*, 773–781.

Roveda, F., Middlekauff, H.R., Rondon, M.U.P.B., Reis, S.F., Souza, M., Nastari, L., et al. (2003). The effects of exercise training on sympathetic neural activation in advanced heart failure – A randomized controlled trial. *Journal of the American College of Cardiology, 42*, 854–860.

Sacknoff, D.M., Gleim, G.W., Stachenfeld, N., & Coplan, N.L. (1994). Effect of athletic training on heart-rate-variability. *American Heart Journal, 127*, 1275–1278.

Sandercock, G.R.H., Bromley, P.D., & Brodie, D.A. (2005). Effects of exercise on heart rate variability: Inferences from meta-analysis. *Medicine and Science in Sports and Exercise, 37*, 433–439.

Schachinger, H., Weinbacher, M., Kiss, A., Ritz, R., & Langewitz, W. (2001). Cardiovascular indices of peripheral and central sympathetic activation. *Psychosomatic Medicine, 63*, 788–796.

Schuit, A.J., van Amelsvoort, L.G.P.M., Verheij, T.C., Rijneke, R.D., Maan, A.C., Sweene, C.A., et al. (1999). Exercise training and heart rate variability in older people. *Medicine and Science in Sports and Exercise, 31*, 816–821.

Sherwood, A., Allen, M.T., Fahrenberg, J., Kelsey, R.M., Lovallo, W.R., & van Doornen, L.J.P. (1990). Methodological guidelines for impedance cardiography. *Psychophysiology, 27*, 1–23.

Sherwood, A., Allen, M.T., Obrist, P.A., & Langer, A.W. (1986). Evaluation of beta-adrenergic influences on cardiovascular and metabolic adjustments to physical and psychological stress. *Psychophysiology, 23*, 89–104.

Sherwood, A., Light, K.C., & Blumenthal, J.A. (1989). Effects of aerobic exercise training on hemodynamic responses during psychosocial stress in normotensive and borderline hypertensive type-A men – A preliminary-report. *Psychosomatic Medicine, 51*, 123–136.

Shi, X.R., Stevens, G.H.J., Foresman, B.H., Stern, S.A., & Raven, P.B. (1995). Autonomic nervous-system control of the heart – Endurance exercise training. *Medicine and Science in Sports and Exercise, 27*, 1406–1413.

Shin, K., Minamitani, H., Onishi, S., Yamazaki, H., & Lee, M. (1997). Autonomic differences between athletes and nonathletes: Spectral analysis approach. *Medicine and Science in Sports and Exercise, 29*, 1482–1490.

Smith, M.L., Hudson, D.L., Graitzer, H.M., & Raven, P.B. (1989). Exercise training bradycardia – The role of autonomic balance. *Medicine and Science in Sports and Exercise, 21*, 40–44.

Stahle, A., Nordlander, R., & Bergfeldt, L. (1999). Aerobic group training improves exercise capacity and heart rate variability in elderly patients with a recent coronary event – A randomized controlled study. *European Heart Journal, 20*, 1638–1646.

Svedenhag, J., Martinsson, A., Ekblom, B., & Hjemdahl, P. (1986). Altered cardiovascular responsiveness to adrenaline in endurance-trained subjects. *Acta Physiol Scand.**[full name please]**, 126*, 539–550.

Svedenhag, J., Martinsson, A., Ekblom, B., & Hjemdahl, P. (1991). Altered cardiovascular responsiveness to adrenoceptor agonists in endurance-trained men. *Journal of Applied Physiology, 70*, 531–538.

Svedenhag, J., Wallin, B.G., Sundlof, G., & Henriksson, J. (1984). Skeletal-muscle sympathetic activity at rest in trained and untrained subjects. *Acta Physiologica Scandinavica, 120*, 499–504.

Task Force of the European Society of Cardiology the North American Society of Pacing. (1996). Heart rate variability: Standards of measurement, physiological interpretation, and clinical use. *Circulation, 93*, 1043–1065.

[may have been cited incorrectly]Uusitalo, A.L.T., Laitinen, T., Vaisanen, S.B., Lansimies, E., & Rauramaa, R. (2004). Physical training and heart rate and blood pressure variability: A 5-yr randomized trial. *American Journal of Physiology-Heart and Circulatory Physiology, 286*, H1821–H1826.

[may have been cited incorrectly]Uusitalo, A.L.T., Tahvanainen, K.U.O., Uusitalo, A.J., & Rusko, H.K. (1996). Noninvasive evaluation of sympathovagal balance in athletes by time and frequency domain analyses of heart rate and blood pressure variability. *Clinical Physiology, 16*, 575–588.

van Doornen, L.J.P., & de Geus, E.J.C. (1989). Aerobic fitness and the cardiovascular response to stress. *Psychophysiology, 26*, 17–28.

Wang, J.S., Jen, C.J., & Chen, H.I. (1997). Effects of chronic exercise and deconditioning on platelet function in women. *Journal of Applied Physiology, 83*, 2080–2085.

Weinstein, A.A., Deuster, P.A., & Kop, W.J. (2007). Heart rate variability as a predictor of negative mood symptoms induced by exercise withdrawal. *Medicine and Science in Sports and Exercise, 39*, 735–741.

Willemsen, G.H., de Geus, E.J., Klaver, C.H., van Doornen, L.J., & Carroll, D. (1996). Ambulatory monitoring of the impedance cardiogram. *Psychophysiology, 33*, 184–193.

Williams, P.T. (2001). Physical fitness and activity as separate heart disease risk factors: A meta-analysis. *Medicine and Science in Sports and Exercise, 33*, 754–761.

Winzer, A., Ring, C., Carroll, D., Willemsen, G., Drayson, M., & Kendall, M. (1999). Secretory immunoglobulin A and cardiovascular reactions to mental arithmetic, cold pressor, and exercise: Effects of beta-adrenergic blockade. *Psychophysiology, 36*, 591–601.

Accepted for publication: June 9, 2008

Annebet D. Goedhart

VU University Amsterdam
Department of Biological Psychology
van der Boechorststraat 1
NL-1081 BT Amsterdam
The Netherlands
Tel. +31 20 598-8787
Fax +31 20 598-8832
E-mail ad.goedhart@psy.vu.nl