Eur J Appl Physiol (2008) 104:557–565
DOI 10.1007/s00421-008-0800-0

ORIGINAL ARTICLE

Effect of physical activity on heart rate variability in normal weight, overweight and obese subjects: results from the SAPALDIA study

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Accepted: 6 June 2008 / Published online: 3 July 2008

Abstract Many studies have demonstrated an association of both a sedentary lifestyle and a high body mass index (BMI) with greater risk for cardiovascular disease. Within the prospective SAPALDIA cohort (Swiss cohort Study on Air Pollution and Lung Diseases in Adults), we investigated whether regular exercise was protective against reduced heart rate variability (HRV), a clinically relevant predictor of cardiovascular morbidity and mortality, and whether adverse effects of obesity and weight gain on HRV were modified by regular exercise. Twenty-four-hour electrocardiograms were recorded in 1,712 randomly selected SAPALDIA participants aged ≥50, for whom BMI was assessed in the years 1991 and 2001–2003. Other examinations included an interview investigating health status (especially respiratory and cardiovascular health and health relevant behaviours including physical activity) and measurements of blood pressure, body height and weight. The association between regular physical activity and HRV and interactions with BMI and BMI change was assessed in multivariable linear regression analyses. Compared to sedentary obese subjects, SDNN (standard deviation of all RR intervals) was 14% (95% CI: 8–20%) higher in sedentary normal weight subjects; 19% (CI: 12–27%) higher in normal weight subjects exercising regularly ≥2 h/week; and 19% (CI: 11–28%) higher in obese subjects exercising regularly ≥2 h/week. Compared with sedentary subjects who gained weight, those who gained weight but did exercise regularly had a 13% higher SDNN (CI: 7–20%). Regular physical exercise has strong beneficial effects on cardiac autonomic nervous function and thus appears to offset the negative effect of obesity on HRV.

Electronic supplementary material The online version of this article (doi:10.1007/s00421-008-0800-0) contains supplementary material, which is available to authorized users.

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Keywords Heart rate variability · Autonomic nervous system · Body mass index · Obesity · Body weight change · Exercise

Introduction

Obesity and weight gain are imposing a growing threat to world health, as in many countries 20–30% of adults are categorized as clinically obese, and their number is still increasing (World Health Organization 1999, 2002). Many studies have demonstrated an association between both a high body mass index (BMI) and a sedentary lifestyle with greater risk for cardiovascular disease (Fang et al. 2003; Wei et al. 1999).

In the SAPALDIA (Swiss cohort Study on Air Pollution and Lung Diseases in Adults) study of a large sample of Swiss adults, we confirmed the relation of reduced heart rate variability (HRV) with increased BMI (Felber Dietrich et al. 2006). Heart rate variability refers to the beat-to-beat variation in heart rate and is a marker of cardiac autonomic control (Kleiger et al. 2005). Reduced HRV predicts increased risk of cardiovascular disease and mortality in longitudinal studies (Bigger et al. 1993; Kleiger et al. 1987). Other studies have noted that increased BMI is associated with reduced HRV, which has been attributed to decreased adreno-receptor responsiveness, withdrawal of parasympathetic tone and/or increased sympathetic activity (Fraley et al. 2005; Ramaekers et al. 1998). Likewise, weight changes have been associated with changes in HRV (Hirsch et al. 1991; Poirier et al. 2003). There is also evidence from the literature that regular moderate endurance training as opposed to strength training has a positive effect on HRV (Hottenrott et al. 2006). Based on these findings, we wanted to test the hypothesis within the prospective SAPALDIA cohort that regular exercise is associated with improved HRV, and that adverse effects of obesity and weight gain on HRV can be modified by regular exercise.

Methods

This study is part of the SAPALDIA cohort study, which was primarily designed to assess health effects from long-term exposure to air pollutants in the Swiss adult population. Details of its design and objectives have been reported elsewhere (Ackermann-Liebrich et al. 2005; Martin et al. 1997). In brief, a random sample of the Swiss adult population was recruited in 1991 from eight areas featuring distinct geographical and environmental conditions. A total of 9,651 participants received intensive health examinations and a detailed health interview in 1991. In 2001–2003, we were able to re-examine 8,047 of the original participants and assess HRV in a random selection ($n = 1{,}846$: 955 women, 891 men) of the 4,417 participants aged $\geq$50 years by 24-h ECGs. Exclusion criteria were as follows: general or spinal anaesthesia within 8 days prior to the ambulatory ECG recording ($n = 5$), having had a myocardial infarction within 3 months prior to the examination ($n = 2$), and taking digitalis ($n = 6$); nobody had an artificial pacemaker. Exclusion of recordings showing atrial fibrillation ($n = 12$), recordings of $<$18 h [recommendations of the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996)] ($n = 73$), and recordings of insufficient quality ($n = 6$) left 1,742 datasets. We had complete information on 1,718 subjects for analysis of HRV involving BMI and exercise and on 1,712 subjects for analysis involving weight gain from baseline to follow-up. For statistical reasons, 15 subjects being underweight at follow-up were excluded from analyses where BMI was used as a categorical variable, leaving 1,703 records for analyses.

HRV measurements and analyses

For the Holter recording, digital devices (Aria, Del Mar Medical Systems, Irvine, CA, USA) with a frequency response of 0.05–40 Hz and a resolution of 128 samples/s were used. Three leads (V_1, altered V_3 with the electrode on the left midclavicular line on the lowest rib, and altered V_5 with the electrode on the left anterior axillary line on the lowest rib) were recorded over 24 h. The mean duration of the Holter recordings was 22.3 (SD 2.1) h.

All recordings were scanned through a StrataScan 563 (Del Mar) and interpreted using the interactive method, with a final visual check on the full disclosure. The length of each RR interval was manually validated during this step. Resampling was made at 4 Hz. Spectral analysis was performed by the fast Fourier transform method. Only normal-to-normal intervals were used, with intervals excluded due to ectopy or artefacts being replaced by holding the previous coupling interval level throughout the time interval to the next valid coupling interval. The standard deviation of all normal RR (NN) intervals (SDNN), which is a summary measure of HRV and the following frequency domain variables have been calculated: total power (TP) ($\leq$0.40 Hz), LF power (0.04–0.15 Hz), high frequency (HF) power (0.15–0.40 Hz) and the LF/HF ratio. HF power is an index of the parasympathetic modulation of heart rate, whereas LF power is an index of the combined parasympathetic and sympathetic modulation of heart rate. LF/HF represents the sympathovagal balance (North American Society of Pacing and Electrophysiology 1996; Sztajzel 2004).

In order to avoid a biased result due to methacholine challenge, which was part of the SAPALDIA lung function testing and which, for practical reasons, was performed before the Holter recording, we excluded the first 2 h of all recordings (van der Woude et al. 2004).

Holter recordings were made between August 2001 and March 2003. Recorders were placed on participants having given consent after a detailed health interview. Participants were asked to follow their regular daily routine and to complete a time-activity diary during the recording period.

Other measurements

Body height and weight were measured with participants not wearing any shoes or coats and body mass index was calculated as weight (kg) divided by height squared (m^2). Four BMI groups were distinguished according to the WHO definitions (World Health Organization 1999): underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2) and obese (≥30 kg/m^2). In the 1991 cross-sectional study, body weight was asked. Weight gain was defined as being in a higher BMI category in the follow-up study compared to the first survey.

The amount of physical activity (Question: 'How many hours a week do you usually exercise such that you get out of breath or sweat?') (The European Community Respiratory Health Survey II 2000) and data on smoking, education, diabetes, level of daytime sleepiness (Epworth sleepiness scale) (Johns 1991, 1993) and current medications status were assessed during a standardized interview which was led by trained fieldworkers. The participants were divided into tertiles of exercise: no regular physical exercise, 1/2–1 h and ≥2 h of regular physical exercise.

Blood pressure was measured twice at rest in the sitting position on the left upper arm by an automatic device (705CP, OMRON, Tokyo, Japan) according to WHO recommendations (World Health Organization 1996). Blood pressure values used in the regression model were obtained by averaging the two measurements. Having high blood pressure was defined as either having a systolic blood pressure >140 mmHg, or a diastolic blood pressure >90 mmHg, or having answered yes to the question "Do you have the following condition: Hypertension?".

The highest degree of education was used as a proxy for social position.

Blood samples were taken from the subjects and known cardiovascular risk factors have been determined by the Institute for Clinical Chemistry of the University Hospital Zürich: a Hitachi Modular Autoanalyser (Rotkreuz, Switzerland) and assays from Roche Diagnostics (Mannheim, Germany) have been used to measure serum levels of uric acid, triglycerides and total cholesterol (all enzymatic tests). High sensitive C-reactive protein (CRP) was measured using a latex-enhanced immunoturbidimetric assay. High-density lipoprotein cholesterol (HDL) was measured with a homogenous assay (Roche diagnostics, Mannheim, Germany) using Roche Cobas Integra (Rotkreuz, Switzerland). HDL values were only used if the participants had a triglyceride level of 9.4 mmol/L or lower. As additional atherogenic markers, the difference between total cholesterol and HDL (non-HDL-cholesterol) and the ratio between total cholesterol and HDL were calculated.

Ethical approval for the study was given by the central Ethics Committee of the Swiss Academy of Medical Sciences and the Cantonal Ethics Committees for each of the eight examination areas and subjects signed an informed consent at the examination.

Statistical methods

Because an initial inspection suggested that the distribution of the residuals was skewed, the HRV-values were log-transformed for further analysis and the results are presented as percent difference between the exposure groups as well as geometric means.

To calculate the effect of BMI and physical activity on HRV, we used a multivariable regression model including variables known from a previous study to influence HRV (study site, sex, age and age squared, education, self-reported diabetes, hypertension, smoking status and beta-blocker intake in the previous 30 days) (Felber Dietrich et al. 2006).

We investigated modification of the effect of BMI by physical activity by introducing according interactions terms between exercise and BMI categories into the multivariable regression model.

Sensitivity analyses screening for additional potential confounders (Epworth sleepiness score >10 vs ≤6; diuretics, sympathomimetics, calcium-channel blockers and angiotensin converting enzyme inhibitor intake during the previous 30 days; non-HDL-cholesterol, uric acid and high sensitive CRP levels) were carried out.

Statistical analyses were performed using Stata 9.2 (Stata corporation, College Station, TX).

Results

Mean age of the population was 60 years (50–73 years). Baseline characteristics of the 1,703 study participants by exercise category are given in Table 1. A sum of 37% of the study population were of normal weight, 43% were overweight, and 20% obese, with a homogeneous distribution across exercise categories. Less than 1% of the study participants were morbidly obese. Between the first

Table 1 Baseline characteristics of the study population ($n = 1,703$)

BMI	Normal weight	Overweight	Obese
n	636 (37%)	723 (43%)	344 (20%)
Female sex	400 (63%)	291 (40%)	180 (52%)
Current smokers	135 (21%)	139 (19%)	58 (17%)
Tertiary education	178 (28%)	189 (26%)	67 (20%)
Diabetes	10 (2%)	27 (4%)	34 (10%)
Beta-blocker intake	40 (6%)	88 (12%)	58 (17%)
Higher BMI cat. in follow-up	17 (3%)	348 (48%)	223 (65%)
No regular exercise	264 (42%)	295 (41%)	152 (44%)
1/2–1 h/week exercise	204 (32%)	243 (34%)	113 (33%)
≥2 h/week exercise	168 (26%)	185 (26%)	79 (23%)
Symptoms of chronic bronchitis	97 (15%)	115 (16%)	60 (17%)
Diuretic intake	8 (1%)	25 (4%)	27 (8%)
Sympathomimetic intake	11 (2%)	29 (4%)	13 (4%)
Calcium channel blocker	13 (2%)	37 (5%)	31 (9%)
ACE inhibitor intake	23 (4%)	49 (7%)	36 (11%)
Mean heart rate (bpm)	74 (SD 9.7)	74 (SD 9.0)	75 (SD 9.1)
Systolic blood pressure (mmHg)	125 (SD 19.0)	136 (SD 18.6)	138 (SD 17.0)
Diastolic blood pressure (mmHg)	78 (SD 10.2)	84 (SD 10.1)	85 (SD 10.0)
Age (years)	59.4 (SD 6.3)	60.8 (SD 6.2)	61.3 (SD 6.1)
Non-HDL cholesterol (mmol/L)	4.6 (SD 1.1)	4.9 (SD 1.2)	4.8 (SD 1.0)
Uric acid (μmol/L)]	288.1 (SD 75.1)	341.8 (SD 79.9)	359.8 (SD 84.1)
C-reactive protein (mg/L)	1.9 (SD 4.5)	2.5 (SD 5.5)	3.9 (SD 5.5)
Epworth sleep score	6.3 (SD 3.6)	6.4 (SD 3.5)	7.0 (SD 3.8)

and the second survey, 35% had gained weight so that they changed into a higher BMI category. There were a higher proportion of women and current smokers in the normal weight group, but fewer subjects with diabetes or subjects taking beta-blockers, diuretics or angiotensin converting enzyme (ACE) inhibitor. In that same group, subjects had lower average heart rate and systolic and diastolic blood pressure, and they were on average better educated and slightly younger; they also had lower levels of non-HDL-cholesterol, uric acid or CRP.

Table 2 exhibits the adjusted means of HRV parameters for different BMI and exercise categories. Within each BMI category, subjects regularly exercising ≥2 h per week had higher HRV than sedentary subjects. Even obese subjects exercising ≥2 h had a higher HRV than sedentary normal weight subjects.

Using a cubic model for BMI (continuous), subjects who exercise regularly had higher SDNN than their sedentary peers (online supplementary Figure 1 showing curves of adjusted geometric means for the three exercise categories). As can be deducted from these curves, SDNN in physically active subjects (≥2 h of exercise per week) did not depend on BMI.

Figure 1 compares SDNN for obese subjects not exercising (reference group) to other BMI and exercise categories. Compared to the reference group, overweight subjects not exercising had an 11% [95% confidence interval (95% CI: 5–17%)] higher SDNN and normal weight subjects not exercising had a 14% (95% CI: 8–20%) higher SDNN.

Regardless of weight, the improvement in SDNN was greatest for those who exercised regularly ≥2 h per week. Compared to the reference group, among those who exercised regularly, SDNN was 19% (95% CI: 12–27%) higher in normal weight subjects, 18% (95% CI: 12–26%) higher in overweight subjects, and 19% (95% CI: 11–28%) higher in obese subjects. The difference in SDNN within each BMI category between subjects exercising regularly ≥2 h and sedentary subjects was highest in obese subjects. Regular exercise modified the relation of obesity with SDNN (95% CI: −0.214 to −0.036 for the difference in the effect of obesity compared to normal weight between subjects exercising regularly (i.e. ≥2 h) and subjects with a sedentary lifestyle) (online supplementary Table 1).

Compared to sedentary obese subjects, obese subjects exercising regularly also had 29% (95% CI: 9–53%) higher total power, 29% (95% CI: 0–66%) higher HF, 27% (95% CI: 4–54%) higher LF (Fig. 2) and a 2% (95% CI: −17 to 16%) lower LF/HF.

Next, we analysed the influence of weight gain between the first survey and the follow-up survey on HRV. Weight gain is defined as changing into a higher BMI category, e.g.

Table 2 Adjusted geometric mean (GM) of HRV in different exercise categories

BMI	Exercise (h/week)	Normal weight		Overweight		Obese	
		GM	95% CI	GM	95% CI	GM	95% CI
SDNN (ms)	None	131.8	(127.5, 136.3)	128.8	(124.9, 132.8)	115.9	(111.0, 121.1)
	1/2–1	135.1	(130.2, 140.2)	131.3	(127.0, 135.8)	127.0	(120.9, 133.5)
	≥2	138.3	(132.8, 144.0)	137.3	(132.1, 142.8)	137.8	(129.9, 146.2)
Total power (ms^2)	None	3,733.2	(3,458.6, 4,029.6)	3,459.4	(3,223.6, 3,712.6)	3,018.3	(2,732.1, 3,334.5)
	1/2–1	3,816.4	(3,504.8, 4,155.7)	3,689.6	(3,415.7, 3,985.4)	3,517.4	(3,141.0, 3,938.8)
	≥2	4,081.3	(3,717.0, 4,481.4)	3,725.3	(3,407.3, 4,072.9)	3,904.0	(3,410.0, 4,469.7)
HF (ms^2)	None	65.1	(58.0, 73.1)	68.6	(61.6, 76.3)	62.0	(53.3, 72.0)
	1/2–1	67.1	(59.0, 76.3)	64.4	(57.4, 72.4)	71.0	(59.8, 84.2)
	≥2	69.1	(60.0, 80.0)	77.1	(67.4, 88.2)	79.8	(65.1, 97.9)
LF (ms^2)	None	206.6	(188.9, 225.9)	217.7	(200.4, 236.4)	167.4	(148.9, 188.1)
	1/2–1	235.2	(212.9, 259.9)	223.2	(203.9, 244.3)	207.4	(181.6, 236.8)
	≥2	247.4	(221.7, 276.0)	240.0	(216.2, 266.5)	211.9	(180.9, 248.4)
LF/HF	None	3.2	(2.9, 3.4)	3.2	(3.0, 3.4)	2.8	(2.5, 3.1)
	1/2–1	3.5	(3.2, 3.8)	3.5	(3.2, 3.8)	2.9	(2.6, 3.3)
	≥2	3.6	(3.3, 3.9)	3.1	(2.8, 3.4)	2.7	(2.3, 3.0)

Adjusted for sex, age, age squared, study site, education, diabetes, hypertension, beta-blocker intake and smoking status

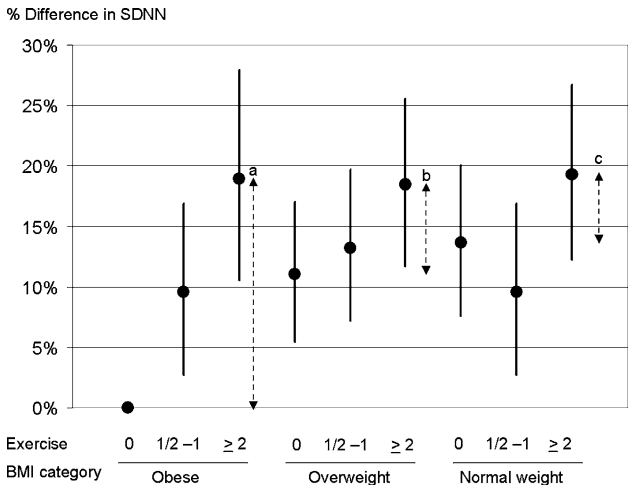

Fig. 1 Compares SDNN for obese subjects not exercising (reference group) to other subject groups stratified by BMI category (normal, overweight, obese) and exercise status. Normal weight is defined as $18.5 \leq$ BMI < 25.0 kg/m^2; overweight $25.0 \leq$ BMI < 30.0 kg/m^2; obese $30.0 \leq$ BMI kg/m^2). Effect estimates and 95% confidence intervals. *a* Difference to sedentary obese subjects. *b* Difference to sedentary overweight subjects (95% CI: −0.196, −0.022). *c* Difference to sedentary normal weight subjects (95% CI: −0.214, −0,036)

becoming overweight or obese. Compared with subjects who gained weight and did not exercise regularly, those who gained weight but did exercise regularly had a 13% higher SDNN (95% CI: 7–20%), 16% higher total power (95% CI: 2–32%), 25% higher HF (95% CI: 3–52%), 24% higher LF (95% CI: 6–44%) and a 1% (95% CI: −14 to 12%) lower LF/HF (Fig. 3).

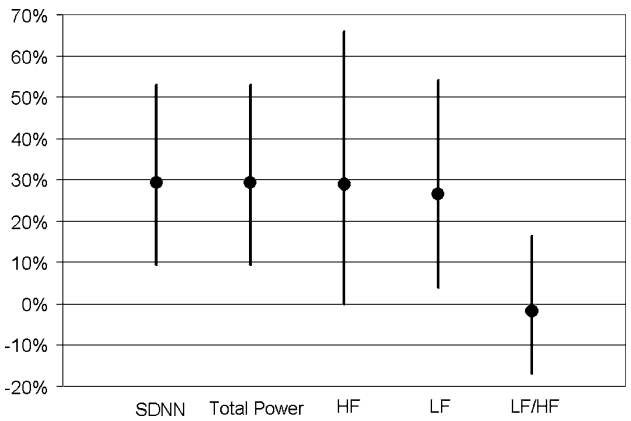

Fig. 2 Average percent increase and 95% confidence interval in measures of HRV (SDNN, total power, HF, LF) in obese subjects exercising ≥2 h/week, compared to sedentary obese subjects

These associations were not due to a reduction in heart rate with exercise as there was no evidence for a change when heart rate was introduced into the models (Table 3). Mean 24-h heart rate in physically active was 74 bpm (95% CI: 72–76 bpm) as opposed to 76 bpm (95% CI: 74–77 bpm) in inactive obese.

Sensitivity analyses

We tested the robustness of the results by including additional potential confounders into the model. Table 3 shows that daytime sleepiness, symptoms of chronic bronchitis, heart rate, cardioactive medication intake or cardiovascular

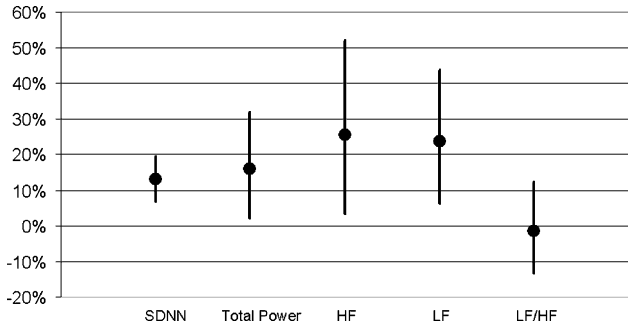

Fig. 3 Average percent increase in measures of HRV (SDNN, total power, HF, LF) in subjects with weight gain exercising ≥2 h/week, compared to sedentary subjects with weight gain. Weight gain is defined as changing to a higher weight category (e.g., becoming overweight or obese)

Table 3 Sensitivity analyses adding different variables to the baseline model with the natural logarithm of SDNN as outcome variable

	Effect estimate[a] (%)	95% CI
Baseline analysis	19	11–28
+ Daytime sleepiness[b]	23	12–35
+ Symptoms of chronic bronchitis[c]	19	10–28
+ Heart rate	16	9–24
+Medication[d]	19	10–28
+ Cardiovascular risk markers in the blood[e]	20	11–29

[a] Estimated %-increase in SDNN associated with regular physical (as compared to a sedentary way of life) exercise in obese, adjusted for sex, age, age squared, study site, education, diabetes, hypertension, beta-blocker intake and smoking status

[b] Epworth sleepiness score >10 vs. ≤6

[c] Questionnaire data: "regular cough or phlegm, during the day or at night"

[d] Diuretics, sympathomimetics, calcium channel blockers, angiotensin converting enzyme inhibitors

[e] Non-HDL-cholesterol, uric acid, high sensitive C-reactive protein

risk markers in the blood did not sizeably change the effect estimates.

We also evaluated whether daytime activity was responsible for HRV differences between populations with higher levels of exercise compared to populations with low levels of exercise. Although the estimates for the sleeping periods at night were different to the ones for the 24-h periods, the relation between the different groups was similar to the one of the 24-h periods, which include active periods (online supplementary Table 2).

Discussion

This study shows that middle-aged and elderly obese subjects who were regularly physically active had a higher HRV than their sedentary peers even after taking into account the effects of sex, age, study site, education, diabetes, hypertension, beta-blocker intake and smoking status. In addition, the improvement in HRV associated with exercise was similar for obese and normal weight subjects. Thus, our data suggest that exercise improves autonomic function as measured by HRV. Analogous to the recently published results of Sui et al. of their study on cardiorespiratory fitness and adiposity as mortality predictors in older adults (Sui et al. 2007), we found that lower autonomic activity among inactive subjects was related to body mass index: inactive subjects who were normal weight had lower HRV than normal weight exercising subjects, but higher than inactive obese subjects.

Several potential sources of bias were considered in this study. Smoking, diabetes or hypertension, all known to have an impact on HRV (Felber Dietrich et al. 2006), were controlled for in the baseline analysis. Obesity is also associated with obstructive sleep apnoea syndrome (OSAS) (Resta et al. 2001), which in turn, has a strong influence on the autonomic nervous system (Narkiewicz and Somers 2003). Even more, obese patients with OSAS who lose weight experience an improvement in the severity of OSAS, as well as in blood pressure and cardiac autonomic regulation (Kansanen et al. 1998). We addressed this issue by additionally controlling for daytime sleepiness in sensitivity analyses but found no indication of such confounding. Furthermore, we were able to demonstrate that the observed differences in HRV between groups were not caused by differences in health status represented by symptoms of chronic bronchitis, intake of cardioactive medication or cardiovascular risk markers in the blood. We also excluded the first 2 h of all recordings in order to avoid a biased result due to methacholine challenge, after which full recovery without application of a beta-agonist takes 33.6 min (1–75 min) (van der Woude et al. 2004). Being a muscarinic receptor agonist, methacholine would lead to an increase in high frequency power.

Our findings are consistent with results from intervention trials comparing the beneficial effects of exercise and weight loss. Oberbach et al. have found that increases in adiponectin levels after 4 weeks of physical training disproportionally exceeded the beneficial effects of reduced percent body fat and increased fitness level (Oberbach et al. 2006). In other studies, 3-month aerobic exercise intervention in overweight and obese subjects increased tissue-type plasminogen activator without evidence of changes in body mass or adiposity (Van Guilder et al. 2005), and 12 weeks of aerobic training improved insulin sensitivity in overweight and obese girls without change in body weight, percent body fat and concentrations of inflammatory markers (Nassis et al. 2005).

There are several limitations of this study. One part of the study was cross-sectional in design, and hence causality cannot be inferred from existing associations. However, we were able to assess weight gain prospectively in the whole population and the fact that weight gain is showing the same effect strengthens the argument for a causal relationship.

Our physical activity data give an overview of the subjects' activity during a relatively recent period; they do not cover lifetime or adulthood exercise. Moreover, they may include anaerobic exercise. The data on physical activity were self-reported, as in most epidemiological studies (US Department of Health and Human Services 1996). Over-reporting of physical activity, the only conceivable form of reporting bias in this context, would have led to an underestimation of the effect size. Nonetheless, the physical activity questionnaire that we used has been previously validated (Washburn et al. 1990), and was used in other epidemiological studies. The comparative study concluded that self-reported sweat hours are suitable for distinguishing active from inactive subjects in epidemiological surveys. Our three activity categories allowed for such a distinction. In the European Community Respiratory Health Survey physical activity level assessed by the same tool was predictive of bronchial hyperresponsiveness (Shaaban et al. 2007). Other studies have used other exercise categories; e.g. the Nurses' Health Study used four categories from zero, moderate, to vigorous exercise, to $\geq$4 h/week of vigorous exercise, showing that women who exercised $\geq$4 h/week had a reduced risk for sudden cardiac death compared to those not being physically active (Whang et al. 2006). The Women's Health Study showed that even as little as 1–1.5 h of light-to-moderate activity are associated with lower coronary heart disease rates (Lee et al. 2001), which puts more emphasis on our results.

A given BMI may not correspond to the same degree of fatness in different people. In addition, the percentage of body fat mass is higher in women than in men for equivalent BMI (Ross et al. 1994). However, different studies have shown that BMI does sufficiently coincide with the degree of body fatness when adjusting for age and sex (Gallagher et al. 1996; Movsesyan et al. 2003). Moreover, the discriminatory power for body fat and lean mass increases with the value of BMI and is high in obese people for whom our results are most pronounced (Romero-Corral et al. 2006).

A major strength of the present study was the large number of participants. Additionally, detailed information was available for numerous cardiovascular risk factors, allowing for control of potential confounders.

In conclusion, our results suggest that regular physical exercise has strong beneficial effects on cardiac autonomic nervous function, a clinically relevant predictor of cardiovascular morbidity and mortality and that exercise may offset the negative effect of obesity.

Funding

The Swiss National Science Foundation (4026-28099, 3347CO-108796, 3247BO-104283, 3247BO-104288, 3247BO-104284, 32-65896.01, 32-59302.99, 32-52720.97, 32-4253.94); the Federal Office for Forest, Environment and Landscape; the Federal Office of Public Health; the Federal Office of Roads and Transport; the canton's government of Aargau, Basel-Stadt, Basel-Land, Geneva, Luzern, Ticino, Zurich; the Swiss Lung League; the canton's Lung League of Basel Stadt/ Basel Landschaft, Geneva, Ticino and Zurich and the National Institute of Environmental Health Sciences (US) (2 P01 ES009825 to DRG, R01 ES011636 to JS).

Acknowledgments The study could not have been done without the help of the study participants, technical and administrative support and the medical teams and field workers at the local study sites.

Local fieldworkers: Aarau: M. Broglie, M. Bünter, D. Gashi; Basel: R. Armbruster, T. Damm, U. Egermann, M. Gut, L. Maier, A. Vögelin, L. Walter; Davos: D. Jud, N. Lutz; Geneva: M. Ares, M. Bennour, B. Galobardes, E. Namer; Lugano: B. Baumberger, S. Boccia Soldati, E. Gehrig-Van Essen, S. Ronchetto; Montana: C. Bonvin, C. Burrus; Payerne: S. Blanc, A.V. Ebinger, M.L. Fragnière, J. Jordan; Wald: R. Gimmi, N. Kourkoulos, U. Schafroth.

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Appendix

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