Physical activity and heart rate variability measured simultaneously during waking hours

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Heart rate (HR) variability (HRV) during ambulatory recordings may be affected by individual differences in daily physical activity (PA). However, the influence of various levels of PA on different measures of HRV is not exactly known. We examined the association between simultaneously measured HRV and objective PA data obtained with an accelerometer during waking hours among 45 healthy adults. Bouts of PA were identified from minute-by-minute accelerometer data as metabolic equivalent (METs) values and calculated as mean METs for 30 min. HRV was analyzed concurrently. Within-individual correlation analyses and sign tests were performed to study the relationships between various HRV indexes and PA. The mean PA time was 15:44 ± 1:01 h, and the mean MET was 1.91 ± 0.14. HR and sample entropy, but not the other measures of HRV, had a significant relationship with PA, as shown by both correlation analyses (r = 0.64, P = 0.021, and r = −0.55, P = 0.022, respectively) and sign tests (P < 0.0001 for both). Beat-to-beat R-R interval fluctuation expressed as SD1 also demonstrated a significant relation to PA according to the sign test (P = 0.037) and a trend of association according to the correlation analysis (r = −0.40, P = 0.129).

The complexity measure of HRV, in addition to average HR and the short-term index of HRV (SD1), is significantly influenced by the level of PA during ambulatory conditions. Long-term HRV indexes remained relatively stable at various activity levels, making them the most robust indexes for the assessment of cardiac autonomic function during free-running ambulatory conditions.

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Heart rate (HR) fluctuations during low-to-moderate changes in physical activity (PA) are predominantly under vagal modulation of the autonomic nervous system (9, 25, 34, 35). Therefore, daily PA may interact and confound the assessment of cardiovascular autonomic regulation during ambulatory monitoring (10, 11). Short-term indexes of HR variability (HRV), such as high-frequency (HF) power or SD1 by the Poincaré plot method, reflect mainly vagally mediated fluctuations of HR (1, 2, 42). Long-term indexes of HRV, such as very-low-frequency (VLF) power or the SD of normal-to-normal R-R intervals (SDNN), are proposed to reveal both vagal and sympathetic influences on HRV (5, 22). Long-term indexes of HRV may also reflect the renin-angiotensin system (38), changes in thermoregulation (24), or changes in daily PA (3, 33, 41). However, the role of PA as a determinant of HRV is not well established.

Depressed HRV, measured from 24-h ambulatory recordings, has been shown to be associated with adverse prognosis in general populations as well as in different patient groups (4, 15–17, 26). More closely, in older studies, long-term indexes of HRV seemed to yield the most powerful prognostic information (6, 21). However, recent studies have shown that HRV methods based on the nonlinear dynamics of HRV provide even more powerful prognostic information among different patient groups (14, 17, 26, 27) as well as among healthy subjects (16, 28). The contribution of PA to the interindividual variation in HRV is not well understood and, to our knowledge, has not been meticulously studied in relation to various spectral and nonlinear dynamics of HRV. Therefore, we examined the relation between simultaneously measured HRV and objective PA data obtained with an accelerometer during waking hours among healthy adults. We hypothesized that PA may contribute significantly to indexes of HRV.

METHODS

Subjects and Experimental Design

The subjects (n = 45) were healthy male (means ± SD; n = 21, age: 35 ± 3 yr, body mass index: 25 ± 2 kg/m²) and female (n = 24, age: 34 ± 4 yr, body mass index: 24 ± 2 kg/m²) volunteers from the city of Oulu, Finland, and its vicinity. All smokers, those who had carried out regular physical exercise training >3 h/wk during the past month, and those with diabetes mellitus, asthma, or cardiovascular disorders were excluded. On their laboratory day (Verve Research, Oulu, Finland), subjects provided written informed consent, completed a health questionnaire, and were assessed for body composition.

An ambulatory R-R interval recording concurrently with PA measurement over a period of 24 h was started. During the measurement day, vigorous exercise was forbidden for practical reasons, e.g., to avoid sweating-caused disturbances to the ECG electrodes and to avoid artifacts caused by moving cables. Otherwise, subjects were instructed to move freely in the way they usually do, e.g., without avoiding normal leisure time- or work-related PA. Use of alcohol and strenuous PA were not allowed on the 2 days preceding the measurement day. The Ethical Committee of the Northern Ostrobothnia Hospital District (Oulu, Finland) approved the protocol.

Assessment of HRV and PA

R-R intervals were recorded over a 24-h period with a Polar R-R Recorder (Polar Electro Oy, Kempele, Finland) at an accuracy of 1 ms (23) and saved on a computer for the further analysis of HR variability with HEARTS software (Heart Signal, Kempele, Finland). The R-R Recorder was connected to the subject via two dermal ECG electrodes; one was placed on the sternum and the other on the left side of the chest. PA data were collected simultaneously with a customized...
Table 1. Baseline characteristics of the study group and HR variability indexes during waking hours

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Men/women</th>
<th>Age, yr</th>
<th>BMI, kg/m²</th>
<th>PA/min, h</th>
<th>METs max</th>
<th>METs std</th>
<th>HR, beats/min</th>
<th>SDNN, ms</th>
<th>HF power, ln ms²</th>
<th>LF power, ln ms²</th>
<th>VLF power, ln ms²</th>
<th>LF-to-HF ratio</th>
<th>SD1, ms</th>
<th>SD2, ms</th>
<th>α₁</th>
<th>SampEn</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>24/21</td>
<td>34 ± 4</td>
<td>24 ± 4</td>
<td>15.44 ± 1.01</td>
<td>2.87 ± 0.44</td>
<td>1.91 ± 0.14</td>
<td>78 ± 9</td>
<td>95 ± 21</td>
<td>5.90 ± 0.74</td>
<td>7.16 ± 0.50</td>
<td>8.21 ± 0.43</td>
<td>1.71 ± 0.47</td>
<td>26 ± 9</td>
<td>132 ± 28</td>
<td>1.36 ± 1.13</td>
<td>0.97 ± 0.15</td>
</tr>
</tbody>
</table>

Values are means ± SD; n = 45 subjects. BMI, body mass index; PA/min, physical activity (PA) time during waking hours; METs max, highest value of metabolic equivalent measured in 30-min epochs during waking hours; SDNN, ms, average value of metabolic equivalent measured during waking hours; HR, heart rate; SDNN, SD of all R-R intervals; HF, high frequency; LF, low frequency; VLF, very low frequency; SD1, beat-to-beat R-R interval fluctuation; SD2, long-term R-R interval fluctuation; α₁, short-term fractal scaling exponent; SampEn, sample entropy.

Polar wrist watch (Polar Electro Oy, Kempele, Finland). Bout of PA were identified from minute-by-minute accelerometer data as metabolic equivalent (METs) values and calculated as mean METs for 30 min. HRV was analyzed concurrently in epochs of 30 min. Individual waking hours were defined on the basis of movements documented by the accelerometer data.

**Time and frequency-domain analysis.** To exclude all undesirable beats, which accounted for <2% of the data in each subject, R-R intervals were edited by visual inspection. We used the deletion method, which simply removes the edited R-R intervals and replaces each removed R-R interval with the following normal R-R interval (36). HRV indexes were calculated from the waking hours that represented active ambulatory daytime. Mean HR and SDNN were used as time-domain measures of HRV. An autoregressive model (model 20) was used to estimate the power spectrum densities of R-R interval variability. Average 30-min values of HR, low-frequency (LF) power (0.04–0.15 Hz), and HF power (0.15–0.4 Hz) were calculated from blocks of 1,024 beats. SDNN and VLF power (0.0033–0.04 Hz) were analyzed over the entire 30-min recording. We analyzed VLF power in longer blocks (block size: 4,096 beats) to be sure that fluctuations in the lowest-frequency (wavelength of 6 min) band of VLF power, which may be affected by PA, were also under investigation (37). The average number of R-R intervals over the 30-min recording that was considered for analysis was 2,323 (range: 1,339–4,019).

**Poincaré plot analysis.** Poincaré plots were analyzed quantitatively using two-dimensional vector analyses in 30-min epochs. Briefly, SD1 measures the magnitude of vagally mediated beat-to-beat variability of the data, and SD2 measures the magnitude of continuous long-term R-R interval fluctuation. Details of the two-dimensional vector analyses have been previously described elsewhere and were used accordingly in the present study (42).

**Analysis of nonlinear HR dynamics.** As nonlinear indexes of HRV in 30-min epochs, again, we analyzed the short-term fractal scaling exponent (α₁) and sample entropy (SampEn). The fractal analysis method differs from traditional measures of HRV because it does not measure the magnitude of variability but rather the qualitative characteristics and correlation features of HR behavior. Briefly, in the fractal analysis, the root mean square fluctuations of integrated and detrended data are measured in observation windows of different sizes and then plotted against the size of the window on a log-log scale. In this study, short-term (from 4 to 11 beats) α₁ was calculated on the basis of previous experiments (17, 28). Details of the fractal scaling method have been previously described elsewhere (29). SampEn is an index of HR dynamics complexity. It quantifies the amount of overall regularity or predictability in time series data. Lower values of SampEn indicate more predictability in the time series compared with higher values (32). In the present study, SampEn was calculated using Kubios HRV software (version 2.0, Biosignal Analysis and Medical Imaging Group, Department of Physics, University of Kuopio, Kuopio, Finland). Two input variables, m = 2 and r = 20% of the SD of the datasets, were fixed as previously described (23, 32) to calculate SampEn.

**PA analysis.** PA data were continuously collected by a Polar wrist watch equipped with a one-dimensional accelerometer. Unlike most commercially available accelerometers, our instrument was tuned to LF movements (0.3–1.5 Hz) and programmed to register movement if acceleration exceeded 0.1 g. The instrument used the pulse-filtering procedure presented in European Patent 1532924. The minute-by-minute movement count was transformed to intensity in METs using a nonlinear relationship and a body height-based calibration factor. Similar technology has been recently validated by measuring energy expenditure using indirect calorimetry, and excellent accuracy was found (8). Similar to HRV parameters, a 30-min average of the intensity level was calculated in METs.

**Statistical Analyses.** Individual correlation analyses for each subject were performed for all major questions. This means that, on average, 31 observations (i.e., 30-min epochs) for all HRV indexes and PA were initially used for each of the 45 subjects. This approach has been previously described by Grossman et al. (11) when they studied the association between respiratory sinus arrhythmia and daily activity. We used mean correlation and P values to show significant associations (P < 0.05) between HRV and PA. Shapiro–Wilk’s test was used to examine the Gaussian distribution of the data. Since some of the within-individual HRV and PA data were skewed, Spearman’s correlation analyses were performed. Moreover, we performed the sing test to strengthen the statistical approach of our study (GrapPad Software, La Jolla, CA). According to the number of subjects, the sign test requires that at least 29 of the 45 subjects demonstrate a significant relation (i.e., correlation with P to the mean). ANOVA was used to compare if the baseline characteristics and mean values of HRV differed between the groups.

Table 2. Mean values of within-individual Spearman correlation coefficients and P values between concurrently analyzed PA and HR variability of the study group

<table>
<thead>
<tr>
<th>Spearman ρ</th>
<th>Significant relation, number of the subjects</th>
<th>P value</th>
</tr>
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<tbody>
<tr>
<td>HR, beats/min</td>
<td>0.635</td>
<td>0.021</td>
</tr>
<tr>
<td>SDNN, ms</td>
<td>0.050</td>
<td>0.368</td>
</tr>
<tr>
<td>HF power, ln ms²</td>
<td>-0.391</td>
<td>0.144</td>
</tr>
<tr>
<td>LF power, ln ms²</td>
<td>-0.135</td>
<td>0.306</td>
</tr>
<tr>
<td>VLF power, ln ms²</td>
<td>-0.031</td>
<td>0.410</td>
</tr>
<tr>
<td>LF-to-HF ratio</td>
<td>0.349</td>
<td>0.164</td>
</tr>
<tr>
<td>SD1, ms</td>
<td>-0.397</td>
<td>0.129</td>
</tr>
<tr>
<td>SD2, ms</td>
<td>0.072</td>
<td>0.357</td>
</tr>
<tr>
<td>α₁</td>
<td>0.397</td>
<td>0.135</td>
</tr>
<tr>
<td>SampEn</td>
<td>-0.548</td>
<td>0.022</td>
</tr>
</tbody>
</table>

The sign test requires that at least 29 of the 45 subjects demonstrate a significant relation, i.e., correlation with P value to the mean.
RESULTS

The mean PA time of the subjects was 15:44 ± 1:01 h during waking hours. The mean maximal MET in 30-min epochs was 2.87 ± 0.44, and the mean MET for the whole epoch of waking hours was 1.91 ± 0.14. The mean METs or mean maximal METs for the waking hours were not related with simultaneously measured mean HR or any mean values of HRV indexes \( [P = \text{not significant (NS) for all}] \). There were also no differences between genders in any baseline characteristics, PA, or any measured HRV indexes. Baseline characteristics of the subjects and mean HRV indexes during waking hours are shown in Table 1.

The mean values of the within-individual correlation analyses showed a significant association between PA and HR \( (r = 0.64, P = 0.021) \) and between PA and SampEn \( (r = -0.55, P = 0.022) \). Short-term indexes of HRV (HF power and SD1) and \( \alpha_1 \) indicated a nonsignificant trend toward an association with PA \( (r = -0.39, P = 0.144; r = -0.40, P = 0.129; \) and \( r = 0.40, P = 0.135, \) respectively). Likewise, the LF-to-HF ratio showed a similar trend toward a relation with PA \( (r = 0.35, P = 0.164) \). Long-term indexes of HRV did not correlate with PA in the entire cohort (Table 2).

The sign tests strengthened the association between PA and HR and between PA and SampEn \( (P < 0.0001 \text{ for both}) \). SD1 also demonstrated a significant relation to PA according to the sign test \( (P = 0.037) \). However, long-term HRV indexes, measured as SDNN, VLF power, and SD2, did not associate with PA \( (P = \text{NS for all}) \). All the mean values of within-individual correlation

Fig. 1. Representative examples of physical activity (PA) during waking hours (top) and associations among heart rate [HR; in beats/min (bpm); \( A \)], HR variability [SD of normal-to-normal R-R intervals (SDNN; \( B \))], high-frequency (HF) power (C), low-frequency (LF) power (D), very-low-frequency (VLF) power (E), and the LF-to-HF ratio (\( F \)), and PA from a subject with high PA. PA is expressed as mean metabolic equivalents (METs) in 30-min epochs. PAtime, PA during waking hours; METsmax, maximum METs; METsav, average METs.
analyses between PA and HRV and the results of the sign tests are shown in Table 2. Representative examples of the PA and HRV data during waking hours from a subject with high PA and one with low PA are shown in Figs. 1 and 2, respectively. In addition, representative examples of SD1, $\alpha_1$, and SampEn data from a subject with high PA and one with low PA (same subjects as in Fig. 2) are shown in Fig. 3.

DISCUSSION

The main finding of this study was that the objective PA data obtained with an accelerometer, measured simultaneously with HRV during waking hours, have significant influence on HR, SD1, and the complexity properties of HR. However, long-term HRV indexes remained relatively stable at various activity levels, making them robust indexes of cardiac autonomic function when HRV is measured during free-running ambulatory conditions. Since altered HRV has been shown to be an independent predictor of mortality in both healthy subjects and various patient groups, the present results may provide important clues to understanding and considering the contribution of PA that underlies the regulation of cardiac autonomic function.

Methodological Considerations

Self-reported questionnaires on PA suffer from significant reporting bias, tending to overestimate PA levels (7, 40). Accelerometers offer a reliable and affordable solution to problems with self-reported data (39). In the present study, we used analogous accelerometers recently validated against indirect calorimetry (8). We performed the spectral HRV analysis in longer data blocks for VLF power to confirm that fluctua-
tions in the lowest-frequency band were not missing from the 30-min analysis. In addition, we wanted to concentrate on observed individual values performed by correlation analyses for each subject separately, since HRV values are highly variable between individuals, even under resting conditions (12, 13, 20). Finally, to confirm our findings, we performed the sign tests to again demonstrate the significant relations. Therefore, we feel that our approach represents a methodological framework for understanding the possible contribution of PA in modifying several indexes of HRV during waking hours.

Association Between PA and Short-Term Indexes of HRV

HR dynamics are closely tied to PA. The higher the average PA, the higher the average HR, which was also clearly observed in the present study. Furthermore, the higher the average HR, the lower the HRV. Taken together, we can expect that changes in PA have evident influences on HRV. Recent studies (10, 11) have shown that markers of cardiac sympathovagal modulation of HR, i.e., short-term HRV indexes, not only reflect individual differences in sympathovagal regulation but also variations in daily PA patterns. Our results are in line with these previous reports. We observed a significant association between short-term R-R interval fluctuation, expressed as SD1 and PA, and also a trend toward an association between PA and HF power and between PA and the LF-to-HF ratio, an index of sympathovagal balance.

Association Between PA and Long-Term Indexes of HRV

Long-term indexes of HRV have also been proposed to be affected by PA (33). However, the marked contribution of PA to HRV has been documented only when spectral power in the ultra-LF band (0.0033 Hz) was analyzed among healthy subjects (3) and among cardiac patients (33). In the present study, we did not analyze ultra-low indexes of HRV, since an epoch of recording >30 min would be needed to capture those fluctuations. We found no marked association between long-term indexes of HRV in terms of SDNN, VLF power (0.0033–0.04 Hz) or SD2, and PA. A recent study by Aoyagi and colleagues (3) studied the effects of PA, food intake, and circadian rhythm on core body temperature-corrected HRV, and they showed results similar to those obtained in the present study. They concluded that HRV, when analyzed in the frequency band ranging from 0.0035 to 0.1 Hz, is independent of behavioral effects, including those in usual daily PA. This is an important note, since it can be suggested that long-term spectral indexes of HRV reflect an intrinsic regulatory system that is not disturbed by PA.

Association Between PA and Nonlinear Indexes of HR Dynamics

A novel finding of the present study is the clear relationship between PA and SampEn. SampEn measures the regularity and
complexity of time series data, and it has proven independent of record length, displaying relative consistency under different circumstances (32). The larger the value of SampEn, the greater the unpredictability in the R-R interval time series. The mean value of SampEn has been shown to be ~1 in healthy adults during 5-min standing conditions (19). We observed similar mean values in the present study during waking hours. Furthermore, it has been previously described that heart complexity decreases during an autonomic vagal blockade by atropine and increases during vagal stimuli by low atropine (31). Similarly, decreased values of SampEn have been observed during sympathetic activation performed by graded head-up tilt conditions (30). The present data show that SampEn is associated with PA under various PA levels. It can be suggested that sympathovagal modulation of HR allows fast adaptability to different circulatory needs at different PA levels, which leads to PA-dependent complex R-R interval signal behavior in daily free-running conditions. This may partly explain the high sensitivity of SampEn to react to changes in PA at the individual level.

Limitations

The present study was limited by the fact that we did not control respiratory activity during the ambulatory measurements. Indeed, short-term HRV indexes are associated with PA due to the fact that during low to moderate PA, the respiratory pattern changes not only in terms of frequency but also in terms of volume. Obviously, controlling breathing rate might have given additional information, since ambulatory respiratory sinus arrhythmia magnitude is associated with PA and vagally mediated indexes of HRV (11). However, our study setup absolutely mimics ambulatory ECG measurement outside the clinic, which may emphasize the practical value of the results. Second, we investigated PA and HR dynamics during modulation of the autonomic nervous system only in healthy subjects. We decided to start with healthy subjects because it may be important to first understand the contribution of PA to HR behavior in a homogeneous sample of subjects. However, most likely, the patient data during ambulatory measurements represent relatively low PA levels. Thus, whether the same findings apply to other population groups and to cardiac patients remains to be confirmed in future studies.

Implications

Reduced HRV during ambulatory monitoring has been shown to be associated with the occurrence of various clinical events. Our results indicate that individual differences in the extent of PA affect short-term and nonlinear indexes of HRV. Therefore, it seems important to consider concurrent monitoring of PA, especially when assessing sympathovagal-mediated indexes of HR. We did not observe a marked relation between long-term indexes of HRV and PA. In this respect, it can be suggested that long-term indexes of HRV may reflect an independent intrinsic regulatory system of the autonomic nervous system that is not affected by PA and may be more suitable for clinical studies assessing cardiac risk from ambulatory ECG recordings. This observation is line with previous studies (6, 18) showing that long-term indexes are stronger predictors of mortality and arrhythmic events than short-term HRV indexes. In summary, PA at the time of ambulatory HR monitoring has influence on short-term HRV indexes and the complexity properties of HR. However, long-term HRV indexes remained relatively stable at various activity levels, making them robust indexes when HRV is measured during free-running ambulatory conditions for prognostic purposes.

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DISCLOSURES

No conflicts of interest are declared by the author(s).

REFERENCES


