Discrimination between Healthy and Sick Cardiac Autonomic Nervous System by Detrended Heart Rate Variability Analysis

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Multiresolution Wavelet Transform and Detrended Fluctuation Analysis have been recently proven as excellent methods in the analysis of Heart Rate Variability, and in distinguishing between healthy subjects and patients with various dysfunctions of the cardiac nervous system. We argue that it is possible to obtain a distinction between healthy subjects/patients of at least similar quality by, first, detrending the time-series of RR-intervals by subtracting a running average based on a local window with a length of around 32 data points, and then, calculating the standard deviation of the detrended time-series. The results presented here indicate that the analysis can be based on very short time-series of RR-data (7-8 minutes), which is a considerable improvement relative to 24-hours Holter recordings.

I. INTRODUCTION

Measurements of Heart Rate (HR) and evaluation of its rythmicity have been used for a long time as a simple clinical indicator. Research from the last decade has indicated that a quantification of the discrete beat to beat variability in HR - the heart rate variability (HRV) - might be a possible prognostic indicator of risk associated with a large variety of diseases, behavioral disorders, mortality and also ageing. For example, independent of other established risk factors, depressed HRV has been shown to be a powerful predictor of cardiac events after myocardial infarct. It is therefore of great importance to establish a measure of HRV and to classify the HRV of different pathological cases in order to discriminate the healthy HRV profile from that for patients at risk [1–4]. It is an open question in the literature if one needs long time series (24 hour ECG Holter data series [5]) or whether short time series (ca. 5 minutes [6]) do suffice in producing a reasonable clear separation between healthy and sick individuals. This question is probably tied up with the quality of the ECG recording, i.e. the signal to noise ratio.

In physiological systems one can recognize different behaviours at different time scales. For example, consecutive heart beats will occur more or less with the same beat-to-beat interval (the mean HR), which can be defined as a small time scale. Other time scales can be defined by the sleep/wake periods. On these larger time scales one can identify a different heart rate and a different heart rate variability during the hours of sleep and during the hours of awakeness. The DFA (Detrended Fluctuation Analysis) [7] and the DWT (Discrete Wavelet Transform) [8–15] have been shown to be succesful ways of analyzing the HRV. Basically, these methods explore the low and the high frequency behaviour of the signal at different time-scales by applying windows of varying lengths. Thus the DWT was used [9] to analyze data from RR measurements and calculating the standard deviation of the transformed data. This standard deviation of the Wavelet coefficients serves as a characterization of the HRV during the period of measurement and it was shown that the method discriminates between healthy and sick individuals. Thuerr *et al* [9] observed a complete separation of the two groups for window sizes 2^4 and 2^5, where the exponent indicates the window scale. Further, this method was used by our group [10] on a different set of data, and the separation mentioned was found not to be complete (see also [16]). In order to improve the method a filtering algorithm was constructed and the standard deviation of the filtered time-series now resulted in a complete separation between healthy and sick subjects. We emphasize that the diagnostic virtue of the DFA and DWT methods apparently is due more to the right choice of window size than to the actual method of transformation. Both of the two methods point to a typical time scale of 2^4 to 2^5 equivalent to a window size of 16 to 32 heart beats. Thus in the DFA method [7] one observes a crossover point for a window size around n=16 heart beats where an abrupt change in the slope of their [7] $F(n)$ vs. n curve occurs.

In this study we wish to see if the existence of this time scale can be utilized for the analysis of HRV of short term ECG recordings.

II. THE DETRENDED TIME SERIES

As mentioned in the Introduction both the DFA analysis and the DWT analysis suggest an intrinsic window of scale m = 4-5, i.e. a window consisting of 16-32 heart beats. In this section we utilize this to perform a detrending in the following way. First, from the time-series of the raw RR-data * a running average is constructed using an interval-length of 2^m †. Next, the running average is subtracted from the original RR-data time series. For $m = 5$ this procedure is illustrated in Fig. 1a, where the solid curve represents the raw RR-data and the dashed curve represents the running average.The difference between the two curves is denoted by r_i and is shown in Fig. 1b. This resultant time-series r_i is here called the detrended time-series (DTS) and represents the fluctuations with respect to the local average. It is hoped that this procedure at least partly will remove noise and slow oscillations which should not directly affect short term HRV [1,3].

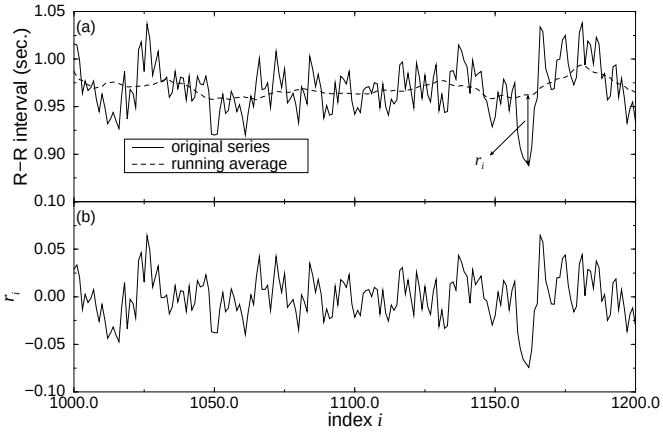

FIG. 1. (a) Segment of RR-interval data versus beat number (solid curve) and running average based on a local window of 32 heart beats (broken curve). (b) Detrended curve, i.e. the difference between solid curve and broken curve in top panel.

The standard deviation σ_d of the detrended time-series (DTS), using a detrending window of scale m, includes now only the behaviour of relevant small time scales and may thus be considered a measure of the HRV. To evaluate the discriminating capabilities of σ_d we examined RR-data for a group of 33 subjects (the same data group as in ref. [10]) consisting of 21 healthy subjects, 9 diabetics and 3 heart patients including one heart transplanted patient. Thus we calculate σ_d for a time-series consisting of $2^{16} = 65536$ data points, corresponding to approximately 16 hours of measured ECG data, and for the scale values m = 1-12 for the detrending window. The smallest length of the detrending window is thus 2 and the largest 4096. The results are shown in Fig. 2, which is the analogous of Figs. 2 and 3 in ref. [10]; the latter two figures. show, respectively, the standard deviation of the wavelet coefficients and of the filtered time series. In the present Fig. 2 one notes a clear separation between the group of healthy subjects (circles) on the one hand, and the groups of diabetics (squares) and heart patients (rhombohedra) on the other hand. However, one also notes from this figure that 3 of the diabetics (the three topmost) with as much justification could have been included in the group of healthy subjects thus displacing the separation region for σ_d towards lower values. For systematic reasons we have chosen the separation region shown in Fig. 2.

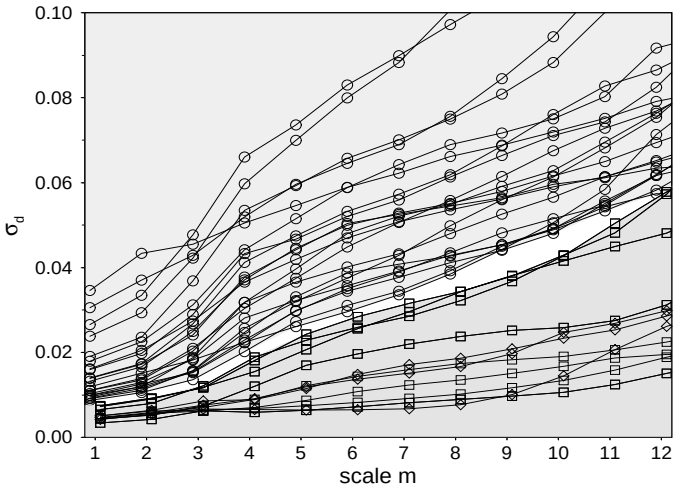

FIG. 2. Standard deviation (in seconds) of the detrended series for a group of 33 subjects versus the scale factor of the local window used in the detrending. Healthy subjects: Circles, Diabetics: Squares and Heart patients: Rhombohedra. The three topmost diabetics have been shown with a special marking.

In Fig. 2 the largest separation betwen the healthy subjects and the two other groups is found for the scale m = 8-11, whereas for the DWT analysis the largest separation was found for the scale m = 4-6, see ref. [10] (see also ref. [16] for discussion of the dependence of the method) and for the DFA analysis the crossover point for the fractal slope was found for the scale $m = 4$, see ref. [7,16]. It should be noted, however, that the crossover point in the DFA analysis is not a sharply defined point, rather the change in fractal slope takes place in a gradual way. On this basis we conclude that the three methods DTS, DWT and DFA yield equivalent estimates for the scale of a characteristic window and in the following we

*An RR interval is the time difference between two consecutive pronounced peaks - the R peaks - of the ECG recording.

†In this study we confined ourselves to an interval length of 2^m, although any interval length can be chosen.

use the scale $m = 5$ [‡].

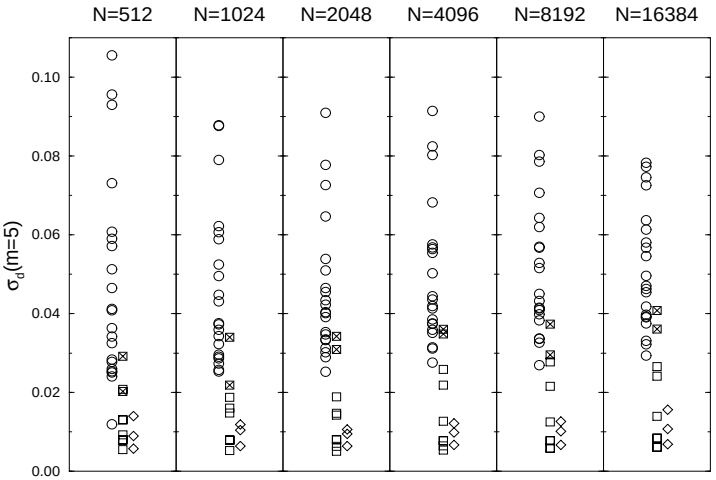

FIG. 3. The standard deviation (in seconds) of the detrended RR-data time-series versus the length of the time series analyzed. Symbols: Same as in Fig. 2

III. ESTIMATION OF INTERVAL LENGTH

In the preceeding section we used an RR-data time-series corresponding to 16 hours of ECG measurements. Clinically it is of course of importance to be able to use as short time-series as possible. In this section we use the DTS method to examine whether or not short time series can be used in order to distinguish between the group of healthy subjects and the groups of diabetics and heart patients. Specifically we choose time-series of lengths 512, 1024, 2048, 4096, 8192 and 16384 data points (RR-intervals). To make sure that all data are collected under similar conditions we have only used data points from the sleep period starting at the initial time 1 a.m. For the various lengths of the time-series we used the same window scale $m = 5$ and the resulting σ_d is shown in Fig. 3. One notes from the figure that for all time-series lengths - including the very short one of 512 measurements corresponding to 7-8 minutes measuring time - an almost complete separation between the different groups (healthy, diabetic and heart patients) is obtained. The only exception is that 2-3 diabetics (marked squares) overlap the group of healthy subjects. As noted in the preceeding section, these diabetics appear to fall in a group for themselves and can with some justification be regarded as belonging to the healthy group of subjects, i.e. as being of no immediate heart risk. Moreover, the entire group of heart patients falls into the lower range of the σ_d scale, $\sigma_d \leq 0.015$ where only a few of the diabetics are found. We remark, that the small number of diabetics and heart patients allows for no definitive conclusion, but we do argue that there are strong indications that even a small length of the RR-data time-series, say 512 measurements, do allow for an almost complete separation between healthy subjects and heart patients/diabetics.

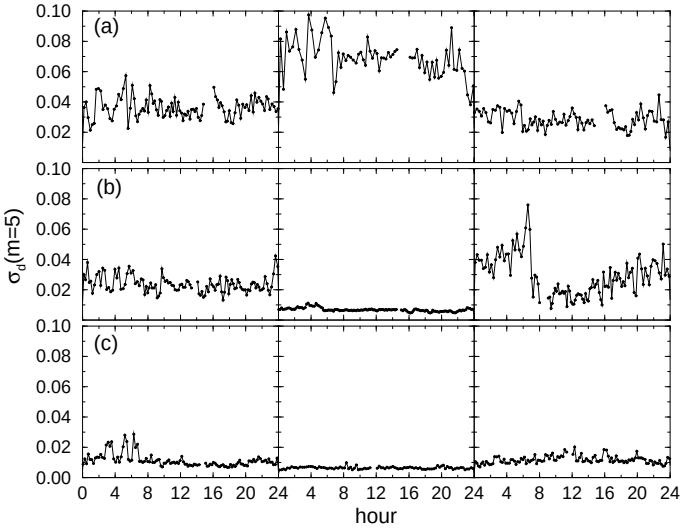

FIG. 4. The daily variation of the standard deviation, calculated for data segments of length 512, versus the time location for the segment. Three representative recordings for each of the groups: (a) Healthy subjects, (b) Diabetics and (c) Heart patients. Again the standard deviation was calculated for the detrended time-series and the scale $m = 5$, i.e. 32 heart beats, was used in the detrending procedure.

IV. DAILY VARIATION OF HRV

We next study the daily variation of the standard deviation of the detrended 24 hour ECG time series. The full data series was divided into smaller segments and in agreement with the conclusion of the preceeding section we choose a segment length of 512 measurements, not including artefacts. Althoguh the daily variation was calculated for all 33 subjects (the same group as in ref. [10]) we here display only 9 representative results. Thus in Fig. 4 we show 3 healthy subjects (top panel, (a)), 3 diabetics (middle panel, (b)) and 3 heart patients (lower panel, (c)) and in all cases σ_d is plotted versus the time position of the data segment. From Fig. 4 one notes, first, that the average value (across 24 hours) of σ_d is far smaller for the heart patients than for the healthy subjects, whereas the diabetics form a more varied population: one (central recording) clearly similar to recordings for heart patients, one (middle panel, third recording) reminiscent of recordings for healthy patients and one (middle panel, first recording) appears to be an in-between case. Secondly, the fluctuation of σ_d during the

[‡]The maximum separation depends on the size of the interval; we have found that $m = 5$ offers the optimal scale for small interval lengths.

24 hours of observation appears to follow the same pattern as just described. We illustrate the above features in two other ways. In Fig. 5 we show the histogram for the daily (24 hours) variation of σ_d for the 3 groups: 21 healthy subjects (circles), 9 diabetics (squares) and 3 heart patients (rhombohedra). For the healthy subjects the maximum of the histogram, i.e. the most probable value of σ_d, is well separated from the maximum of the two other histograms and there is very litlle overlap with the histogram for the heart patients but some overlap with the histogram for the diabetics group. The histograms thus clearly distinguish between healthy and sick subjects, but the statistics is too poor to distinguish between the two patient groups. Finally, in Fig. 6 we show the group average of σ_d for each of the three groups versus the time position for the relevant data segment. In Fig. 6b we have shown the standard deviation (across the group) of the group average of σ_d. From Fig. 6a it follows that the healthy group is separated from the heart patient group by a factor of around 4 in the average of σ_d, a conclusion supported by the standard deviations shown in Fig. 6b. It is also tempting to draw the conclusion that the diabetics group is separated from the heart patient group by 25-50%, however the standard deviations shown in the bottom panel do not allow for a definite conclusion. It also appears from Fig. 6, that the group average value of σ_d is larger during the sleep period, say from 2 to 7 hours, for the healthy group and partly also for the diabetics group (see also [17]). For the healthy group the difference between the sleep and wake period is around 0.01 s.

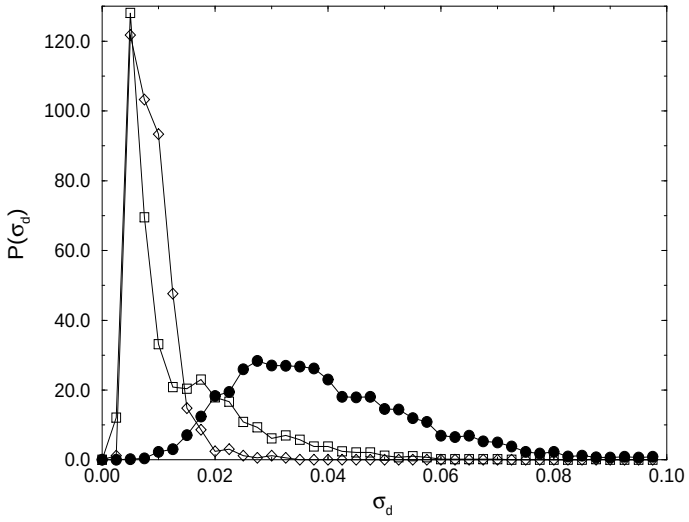

FIG. 5. Histograms for the daily variation of the standard deviation (segment length and scale m as in Fig. 4) shown for the three groups: Healthy subjects (circles), Diabetics (squares) and Heart patients (rhombohedra).

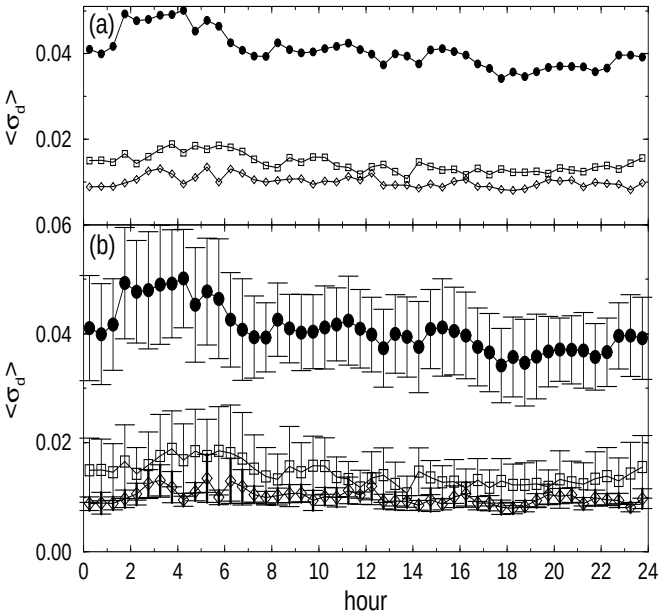

FIG. 6. (a) The group average of the standard deviation (parameters as in Fig. 4.) versus the time location for the data segment. Healthy subjects: circles, Diabetics: squares and Heart patients: rhombohedra. (b) Same as (a), but with the standard deviation across the group indicated by vertical bars.

V. CONCLUSION

In this paper we have focused on the standard deviation σ_d of detrended RR-data time-series using a detrending window with a length 2^5 measurements of RR-data, this value being indicated by results from DWT and DFA analyses, see refs. [10,7]. Our results suggest that even a short time-series of 512 data points, i.e. 7-8 minutes of measurements, suffices to distinguish between healthy subjects and patients (heart disease, diabetics) . The same kind of analysis can of course be performed on the raw, not detrended data [4]. We have done so, but find that using detrended data series are more succesful. We note, that even if the length of the RR-data time-series would have to be increased to, say, 2048 measurements corresponding to app. half an hour of ECG measurements, this would still from a clinical point of view represent a substantial advantage relative to 24 hours of ECG measurements.

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