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**Research Communication**

# Cardiac Inter-Beat Interval Complexity Is Influenced By Physical Activity

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## Abstract:

The complexity of physiological signals may be a more sensitive indicator of health than standard or average measurements. We examined cardiac inter-beat intervals of healthy subjects who are either physically active or sedentary to determine whether measures of complexity are more sensitive to subtle cardiac changes than standard measures. Subjects were pre-screened by self-report, and qualifying subjects were placed in either the active group ($n$ = 10) or sedentary group ($n$ = 10). Cardiac inter-beat intervals were recorded and subsequently analyzed using standard time and frequency domain heart rate variability measurements as well as multiscale entropy and the detrended fluctuation analysis, both measures of complexity. Of the measurements, the detrended fluctuation analysis was the only tool that significantly ($P$ = 0.04) differentiated between the active and sedentary groups. This suggests that the complexity of physiologic signals is a more sensitive indicator of cardiac health than standard measures.

**Abbreviations:** DFA – detrended fluctuation analysis; ECG – electrocardiogram; HRV – heart rate variability; MSE – multiscale entropy; RR interval – cardiac inter-beat interval.

## Introduction:

The emergence of the field of non-linear dynamics, or chaos theory, in the last few decades has re-shaped much of scientific thought. We now know even fairly simple systems can exhibit complex behavior. In fact, in many systems there is such sensitivity to initial conditions that even insignificant noise can completely change their long-term predictability. Such chaotic systems are very unpredictable, but they are still deterministic and therefore not random. Non-linear systems tend to produce data that is somewhere between the predictable simplicity of linear systems and the unstructured nature of truly random systems. This middle ground, where data is unpredictable, yet has “meaningful structural richness,” [Grassberger, 1991] is sometimes termed *complexity*.

The prevailing method in studying physiological systems has been to average the output data. West [2006] argues that averaging data can eliminate important, complex information embedded within the data. Using non-linear analysis tools in place of averages can help uncover information from complex physiologic signals that is otherwise lost. Studies using non-linear tools like the detrended fluctuation analysis (DFA) and the multiscale entropy (MSE) analysis show that data from healthy physiologic systems often contain a high degree of complexity while data produced by pathologic systems often have decreased complexity [Goldberger et al., 2002; Peng et al., 1995; Richman et al., 2000; West, 2006]. West [2006] suggests that the complexity of physiologic systems may be affected by pathology before there is any noticeable difference in the average of the systemic output data. A high degree of complexity within physiologic signals, then, may be a better indicator of health than average values.



Complexity in cardiac inter-beat (RR) interval data, as measured by DFA and MSE, is associated with cardiac health, and a decrease in complexity is associated with cardiac pathologies [Goldberger et al., 2002; Peng et al., 1995; West, 2006]. Inasmuch as regular exercise has a positive impact on cardiovascular health, this study was designed to address the concept of a relationship between RR interval complexity and physical activity. Rather than contrasting healthy versus unhealthy subjects, this study examined healthy young adults who are either physically active or sedentary to determine whether a subtle, sedentarily-induced decrease in cardiac health could be demonstrated by altered complexity in RR interval data.

Tulppo et al [2003] have shown that the DFA $\alpha_1$ value of sedentary subjects decreased after participating in eight weeks of aerobic training, indicating stronger fractal correlations and increased complexity in their heart rate dynamics. Heffernan et al. [2008] had similar results. The present study focuses on the effects of long-term (> 1 year) aerobic exercise habits and includes MSE as a complementary means of measuring complexity. We hypothesized that the heart rate dynamics of healthy young adults who are physically active will exhibit a higher degree of complexity than healthy young adults with a sedentary lifestyle.

## Methods:

***Subjects.*** Male and female subjects were recruited from the local university student population and gave written informed consent via a document approved by the University Human Subjects Institutional Review Board. Subjects self-reported physical activity level by filling out a questionnaire [Appendix A]. The questionnaire was created by the authors for use in the present study and had not yet been tested for validity in its ability to precisely identify a person's level of physical activity. Nevertheless, because the study called for two widely separated groups – either highly active or highly sedentary – rather than a spectrum of physical activity levels, the questionnaire's ability to precisely quantify physical activity level was considered relatively unimportant for the present study. Subjects were invited to participate in the study if they had no serious health conditions, were between the ages of 18 and 40, and were either active or sedentary as defined by the questionnaire.

The physically active group ($n$ = 10; 8 females) included those who participated in aerobic exercise for a period of at least a half an hour with enough intensity to break a sweat at least 3-4 times each week, and had been doing so for more than one year. The age range of the physically active group was 20-26 years with a mean of 22 (SD 2.1). The body mass index ranged between 20.2 and 27.5 kg/$m^2$ with a mean of 22.4 (SD 2.5).



The physically sedentary group ($n$ = 10; 7 females) included those who participated in aerobic exercise for a period of at least a half an hour with enough intensity to break a sweat one time or less each month, and had been doing so for more than one year. The age range of the sedentary group was 21-39 years with a mean of 25 (SD 5.6). The BMI range for the sedentary group was 18.7-28.2 kg/$m^2$ with a mean of 23.8 (SD 3.6). There were no smokers in either group.

***Data Collection and Analysis.*** Data collection took place between 0800 and 2100 hours in a temperature-controlled room. Subjects were asked to refrain from alcohol and caffeine consumption for 6 hours prior to their data collection appointment. Upon arrival, subjects were instrumented with a Polar heart rate monitor chest belt transmitter, and then rested in a seated position for approximately 20 minutes. Immediately following the rest period, RR intervals were recorded for a mean of 8427 (SD 158) heartbeats (or approximately 2 hours) using the Polar S810i (Polar Electro Oy, Kempele, Finland) while subjects rested quietly in the seated position. Although we did not make electrocardiogram (ECG) recordings in this study, Gamelin et al. (2006) have shown that HRV parameters calculated from artifact-corrected data collected by Polar heart rate monitors correlated very well with HRV parameters calculated from ECG recordings. Subjects remained awake during the recording period and were allowed to read or do homework, but they refrained from any external stimuli such as movies or music.

Following data collection, the RR interval data was converted to text format using the Polar Precision Performance SW software (Polar Electro Oy, Kempele, Finland). Data sets were then plotted and manually inspected for artifacts (any obviously abnormal spikes on the graph). All artifact data points (mean of 0.48%, SD 0.58%, range 0.0-2.16% of total data points in all subjects) were subsequently deleted from the data sets so that no obvious spikes appeared on a plot of the data. For each subject, the publicly available DFA and MSE software [Goldberger et al., 2000] were used to analyze the data, and Matlab (The Mathworks, Inc., Natick, Maryland) was used to plot the MSE output, plot the DFA output, and calculate the DFA $\alpha_1$ value.

Standard heart rate variability (HRV) measures, including SDANN, RMSSD, NN50, pNN50, VLF, LF, HF, LF/HF, and Poincare SD1, SD2, and SD1/SD2, were calculated using HRV Analysis Software version 1.1 [Professor Pasi A. Karjalainen, University of Kuopio, Finland]. The standard lengths of RR data sets for these HRV measures are 5 minutes or 24 hours, depending on the measure [Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology, 1996]. In the present study, we recorded data for a non-standard interval of 2 hours, so our HRV analysis values should not be compared to values from other studies. We were primarily interested in determining the effectiveness of standard HRV measures to discriminate between the active and sedentary groups.



***Measuring Complexity.*** DFA and MSE are non-linear tools that can measure complexity in time series data. In contrast to periodic/linear or random time series, complex time series often have correlations across time scales, i.e., small fluctuations at small time scales have similar characteristics to large fluctuations at large time scales. Both the DFA and MSE test for correlations across temporal scales.

The DFA [Peng et al., 1994; Peng et al., 1995; Goldberger et al., 2000] has been described as a quantitative measure of stochastic self-similarity, or fractal correlation, in time series data characterized by a scaling exponent, $\alpha$. While the physiological basis for the DFA $\alpha$ value is not well understood, the $\alpha$ scaling exponent has, nevertheless, proven useful in cardiology. Fractal correlations (an $\alpha$ value of 1.0) have been associated with healthy heart rate dynamics, and a loss of fractal correlations is associated with disease and aging [Goldberger et al., 2002]. The short-term DFA scaling exponent, $\alpha_1$ [see Peng et al., 1995 for further explanation of $\alpha_1$], has been shown in some studies to increase toward 1.5 as age increases [Goldberger et al., 2002; Iyengar et al., 1996]. The $\alpha_1$ value is also considered the most reliable predictor of mortality in post-myocardial infarction patients—an $\alpha_1$ approaching 0.5 for those with high mortality risk [Stein & Reddy, 2005].

Despite the use of the DFA $\alpha_1$ as a measure of the fractal correlation, and thus the complexity of a given time series, there is some controversy as to whether the DFA $\alpha_1$ is actually measuring complexity. Willson et al. [2002] and Francis et al. [2002] argue that DFA α values are simply frequency-weighted forms of the ratio of low-frequency (LF) to high-frequency spectral power of RR intervals [LF/HF] or LF/(HF+LF), and thus provide no information beyond what conventional spectral analyses show. Nevertheless, other researchers [Peng et al., 1995, Goldberger et al. 2002, and Tulppo et al. 2005] hold to the assertion that the DFA α quantifies the fractal correlations embedded in RR interval time series data, thus reflecting cardiac complexity generated by delicate interactions of sympathetic and parasympathetic influence on the RR intervals. For the purposes of this study we have adopted the often-used latter view of the DFA α as a measure of fractal correlations.

MSE [Costa et al., 2002; Costa et al., 2005; Goldberger et al., 2000] is also a measure of complexity. It measures the entropy [Richman et al., 2000], or rate of information production, of time series data over varying scales. MSE has not been used in cardiology to the same degree as DFA, so its value in HRV analysis has not yet been established. Additionally, because complexity as measured by MSE does not return a single value metric like the DFA or the standard HRV measures, it is more difficult to use for statistical comparisons. However, MSE plots associated with healthy cardiac dynamics have been shown to have constant entropy across scales, while the MSE plots of people with atrial fibrillation, congestive heart failure, or people who are elderly vary with scale [Costa et al., 2002; Costa et al., 2005].



## Results and Discussion:

Results are summarized in *Table 1 (next page).* The data generated by each HRV measure were subjected to statistical *t*-tests to determine each measure's sensitivity in identifying a difference between the active and sedentary groups, as indicated by a lower *P* value ($P < 0.05$ being considered significant). Of all measures tested, the DFA was the only one to achieve statistical significance, though others were close. Because the data sets were small (n=10 for each group), data were log transformed and re-evaluated using a statistical *t*-test to stabilize variance. While some measures improved in statistical significance with transformed data, the DFA was still the only measure with $P < 0.05$. The spectral ratios of the low frequency (LF) to high frequency (HF) spectral power of RR intervals [LF/HF] and LF/(HF+LF) ($P = 0.09$ and 0.08, respectively), suggested by Willson et al. [2002] and Francis et al. [2002] to be essentially equivalent to DFA $\alpha_1$, were notably less statistically significant than the DFA $\alpha_1$.

The DFA analysis indicates that healthy young adults who are physically active have a higher degree of cardiac complexity than healthy young adults who are physically sedentary. Our measured mean $\alpha_1$ value for the sedentary group was 1.20 compared to 1.02 for the physically active group (a value of 1.0 represents maximum complexity as measured by the DFA). For older, healthy adults, $\alpha_1$ values tend to approach 1.5 [Goldberger et al., 2002; Iyengar et al., 1996] indicating that the sedentary group appears "older" in terms of cardiac complexity.

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**Table 1:** Comparison of several HRV measures in their ability to differentiate between RR interval data of active vs. sedentary subjects, as indicated by a statistical *t*-test *P* value.

| Parameter | **Sedentary Subjects** *Mean (SD)* | **Physically Active Subjects** *Mean (SD)* | *P* Value | *P* Value (for log transformed data) |
|---|---|---|---|---|
| DFA$\propto$1 | 1.20 (0.16) | 1.02 (0.20) | 0.04 | 0.04 |
| SDANN | 0.060 (0.015) | 0.077 (0.032) | 0.14 | 0.16 |
| RMSSD | 43.5 (18.2) | 70.0 (42.0) | 0.08 | 0.06 |
| NN50 | 873 (623) | 1390 (945) | 0.17 | 0.20 |
| PNN50 | 21.0 (15.2) | 33.4 (22.7) | 0.17 | 0.20 |
| VLF | 568 (274) | 847 (600) | 0.20 | 0.35 |
| LF | 829 (348) | 1189 (867) | 0.24 | 0.42 |
| HF | 418 (376) | 1181 (1541) | 0.15 | 0.06 |
| LF/HF | 3.2 (2.3) | 1.7 (1.3) | 0.09 | 0.08 |
| LF/(HF+LF) | 0.69 (0.15) | 0.56 (0.16) | 0.08 | 0.07 |
| Poincare SD1 | 31.2 (13.0) | 50.2 (29.8) | 0.08 | 0.06 |
| Poincare SD2 | 97.2 (19.3) | 121.3 (48.9) | 0.17 | 0.22 |
| Poincare SD1/SD2 | 0.31 (0.09) | 0.40 (0.11) | 0.07 | 0.07 |
| Heart rate | 72.8 (6.76) | 66.1 (10.2) | 0.10 | 0.08 |

DFA – detrended fluctuation analysis; SDANN – standard deviation of the averages of RR intervals; RMSSD – root mean square of successive differences in RR intervals; NN50 – number of adjacent RR intervals that differ by more than 50 ms; PNN50 – proportion of adjacent RR intervals that differ by more than 50 ms; VLF, LF and HF are absolute values of very low frequency, low frequency and high frequency spectral powers of RR intervals; SD1 and SD2 are standard deviations 1 and 2 - Poincare plot descriptors.
The only statistically significant measure ($P < 0.05$) was the DFA. Data were also log transformed to stabilize variance, and the transformed data were subjected to *t*-tests, the *P* values of which are included. While some measures showed improvement, the DFA is still the only measure with statistical significance.

Our sedentary group did include one subject who was older than any subject in the active group, which theoretically could have confounded the DFA results, resulting in a false association between physical activity and the DFA $\alpha_1$ value. However, when the data of that subject was removed from the analysis, the statistical significance of the DFA as a differentiator not only held up, but improved ($P = 0.03$). The DFA results were therefore not a result of age-related confounding.

Complexity as measured by the MSE analysis, unlike the DFA, cannot be characterized by a single number; rather complexity is indicated by the shape of the graph. Previous physiological applications of the MSE focused on differentiating between healthy and pathological conditions, which it did well in many cases. In our study, however, both groups were healthy – individuals in either group had no known pathological conditions. In our case, the MSE shows approximately equal levels of complexity in both the active and sedentary groups. Both the DFA and MSE successfully identified levels of complexity in the active and sedentary groups that are consistent with good cardiac health, but the MSE does not capture the differences between the two groups.

It is important to note, greater levels of physical activity were more strongly associated with a lower DFA $\alpha_1$ scaling exponent ($P = 0.04$) than with any of the standard measures of HRV ($P > 0.05$ for all standard measures), even after stabilization of the data by log transformation. These results suggest that subtle differences in cardiac health are better detected by a change in the complexity of heart rate dynamics, as measured by the DFA in this study, than by more traditional methods.



The better sensitivity of the DFA versus traditional measures carries with it some practical implications. While it has been shown that traditional HRV measures used on electrocardiogram-derived data can successfully differentiate between physically active and sedentary men in a highly controlled environment [Melanson, 2000], it is not practical for most fitness and training facilities to so tightly control the environment when their clients are analyzed. The present study suggests that the DFA can successfully differentiate between active and sedentary people, even when the environment is noisy – a much more realistic scenario in the real world. Moreover, the data for this study was taken for a relatively short period of time using a simple, widely available heart rate monitor rather than an electrocardiogram recording. Therefore, the DFA may be a more practical tool in fitness analysis.

The DFA may also have practical clinical applications. If, as the results of the present study suggest, the early stages of cardiac pathology are better detected by altered HRV complexity rather than by traditional HRV measures, clinicians could use the DFA as an early indicator of risk for cardiac pathology. An earlier detection of at-risk cardiac patients via the DFA may help facilitate earlier intervention and, therefore, possibly better outcomes.

The results of this study may also have some philosophical implications. A movement is emerging in physiology away from using averages to smooth out physiologic fluctuations, and toward using non-linear tools to study complex information contained within the fluctuations [Goldberger et al., 2002; West, 1990; West, 2006]. The term "homeostasis" suggests a simple, static physiologic state associated with health. A more fitting term may be "homeodynamics" [West, 1990] to reflect the complexity in fluctuations associated with healthy systems and the loss of complexity in pathologic systems—regardless of the average values for either system. The results of the present study support the paradigm of homeodynamics. Our results provide evidence that low levels of physical activity affect the complex dynamics of HRV before they affect the broad, traditional values such as average heart rate.

The scientific community has become expert at breaking systems down into their easily observable pieces and learning details about each piece. Problems sometimes arise, however, in trying to accurately rebuild complex systems out of the reduced pieces. Rather than trying to over-simplify inherently complex physiologic systems, more studies should analyze the behavior of entire systems using ideas and methods from the field of non-linear dynamics. Because it appears that pathology presents itself as a change in the complexity of a system before it presents in systemic averages, tools that analyze the complexity of physiologic signals should be able to detect the onset of pathology earlier than systemic averages can. Therefore, emphasis in future studies should be placed on characterizing the differences in complexity of various pathologies compared to healthy complexity, as well as developing more tools for the analysis of complex physiologic information.



***Limitations.*** The foremost limitation of this study is the small sample size. Although we have reported the DFA to be a more sensitive measure than traditional HRV measures based on its lower P value generated from statistical *t*-tests, factors like high variance, age differences, and slightly differing male-to-female ratios between the groups have the potential to impact results when statistical analyses are done on small sample sizes. Nevertheless, the results of the present study provide enough evidence to warrant the execution of larger studies that could provide more statistically robust confirmation of the usefulness of the DFA, or other measures of complexity, as sensitive measures of cardiac health.

Another limitation of this study is the lack of ECG recordings to provide a more-thorough analysis of the recorded RR intervals (e.g. identifying and differentiating recording artifacts from ectopic beats). Although Gamelin et al. [2006] showed ECG data and Polar heart rate monitor corrected data correlated very well, this study lacks the ECG recordings to confirm the same correlation in our data. Therefore, small variations and / or incorrectly identified or missed artifacts in our data derived from the Polar heart rate monitor could have impacted parameters that are sensitive to short-term variability (e.g. RMSSD, DFA$\propto_1$, and SD1).

***Practical Implications*:** A new heart rate analysis tool can use simple data from a widely available heart rate monitor to effectively differentiate between active and sedentary people, even in a noisy environment. The heart rate analysis tool is more sensitive to subtle differences in cardiac health than standard measures, so it could be used clinically for earlier risk assessment, leading to earlier intervention and possibly better outcomes.

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**Contributors:** Benjamin Wilson was primarily responsible for the design, execution, and report of this study. Gus Hart assisted in research design, data analysis, and preparation of the manuscript. Allen Parcell assisted in research design, data collection, and preparation of the manuscript

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## Appendix A:

**Research Questionnaire**

________ I have read and signed the consent form prior to filling out this questionnaire. (Please initial)

________To the best of my knowledge, I have no serious health conditions, i.e. any condition (Please initial) that requires continuing treatment from a health care provider (examples include: heart disease, diabetes, asthma, epilepsy, stroke, cancer, etc.).

Age________

Sex: Male / Female (Circle one)

Height_________

Weight_________

Approximately how often do you do aerobic exercise for a period of at least ½ hour with enough intensity to break a sweat? (Circle one)
1. 5 or more times each week
2. 3-4 times each week
3. 1-2 time each week
4. 2-3 times each month
5. 1 time each month
6. Less than 1 time each month

For approximately how long have you had the exercise habits circled above? (Circle one)
1. More than 2 years
2. 1-2 years
3. 9-11 months
4. 6-8 months
5. 3-7 months
6. 1-2 months
7. Less than 1 month

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