Decreased Fractal Correlation in Diurnal Physical Activity in Chronic Fatigue Syndrome

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Summary

Objectives: Our objectives were to study the temporal correlation of physical activity time series in patients with chronic fatigue syndrome (CFS) during normal daily life and to examine if it could identify the altered physical activity in these patients.

Methods: Fractal scaling exponents of diurnal and nocturnal physical activity time series in 10 CFS patients and 6 healthy control subjects (CON) were calculated by the detrended fluctuation analysis (DFA) and the wavelet transform modulus maxima (WTMM) method. We hypothesized that, due to their illness- and/or fatigue-induced resting episodes, altered physical activity patterns in CFS patients might be observed at the interruption of activity bursts. Thus, we further developed a new method, the wavelet transform negative modulus maxima (WTNMM) method, which could evaluate the temporal correlation at the interruption of activities. We compared the fractal scaling exponents for CFS and CON by each method.

Results: Both for CFS and CON, we found the fractal time structures in their diurnal physical activity records for at least up to 35 minutes. No group difference was found in nocturnal activities. The WTNMM method revealed that, in diurnal activities, CFS patients had significantly ($p < 0.01$) smaller fractal scaling exponent (0.87 ± 0.03) compared to controls (1.01 ± 0.03). Such a difference was identified neither by the DFA nor WTMM method.

Conclusions: CFS patients had more abrupt interruptions of voluntary physical activity during diurnal periods in normal daily life, probed by the decreased correlation in the negative modulus maxima of the wavelet-transformed activity data, possibly due to their exaggerated fatigue.

Keywords

Chronic fatigue syndrome, physical activity, detrended fluctuation analysis, wavelet transform modulus maxima method

Methods Inf Med 2004; 43: 26–9

1. Introduction

Human physical activity is a combined output of not only physiological but also psychological processes that have complex regulating mechanisms. Thus, decreased and/or altered patterns of physical activity have been used to identify/diagnose patients with psychiatric diseases [1, 2] and with a debilitating illness such as chronic fatigue syndrome (CFS) [3, 4]. In these studies, gross measures such as total amount of activity and cumulative distribution of activity counts have been used. Surprisingly, however, up to now there has been no attempt to quantify the time correlations of the fluctuations in the levels of physical activity, which are considered to reflect ongoing regulatory processes more directly, and their alteration by psychiatric and/or psychosomatic disorders, except for one preliminary report suggesting the possibility that activity time series of some manic-depressive patients may show temporal fractal correlations [5].

Recent studies [6, 7] indeed indicated scale-invariant dynamics in physical activity time series with the power-law fractal correlation in their "microstructures" within about an hour. Amaral et al. [7] showed that the constrained activity in healthy individuals, mimicking the decreased activity in bipolar depression and seasonal depression [1] and in CFS [3, 4], significantly decreased the fractal scaling exponent. This suggests a possibility that the fractal index characterizing the fractal scaling of the physical activity time series may be an additional probe [1] of the abnormal patterns of patients with psychiatric and/or psychosomatic disorders.

In this paper, we show that the fractal scaling exponent of physical activity time series is smaller in patients with CFS compared to healthy control subjects (CON). We consider that, in physical activity time series, the temporal correlation of activity bursts and that related to the interruption of activities may have different physiological meanings; we hypothesized that CFS patients, due to their illness- and/or fatigue-induced resting episodes, might show the altered temporal correlation at the interruption of activity bursts. In this paper, we thus propose a new modification of the existing "fluctuation analyses" [8–10] and show that fractal correlation is different between CFS and CON only at the interruption of physical activity bursts.

2. Methods

2.1 Protocols

Physical activity data were collected for 14 days from 10 CFS patients and 8 control subjects. All the patients were outpatients of the University Medical Centre Nijmegen, The Netherlands and fulfilled the Center for Disease Control criteria for CFS [11]. The CFS patients used in this study were those who are characterized by pro-

found physical inactivity and categorized as "pervasively passive" CFS by van der Werf et al. [4]. We also studied activity records of "active CFS" patients with comparable amounts of activity as healthy controls, but found no significant difference in the scaling properties. The data collection device (Actilog V3.0) was worn on the ankle during usual daily life. Acceleration counts above a threshold level were integrated for every 5 min. Further details of the subjects and the device are described elsewhere [4]. The data for the first and the last days were excluded to obtain 12 complete days for analyses. A day with missing data, with continuous zeros for more than 100 min during diurnal and 3 hours during nocturnal periods, was dropped. As a result, two control subjects were excluded for lacking 12 days. Therefore, the data from 10 CFS and 6 control subjects were used in this study.

Because temporal correlations in physical activity have been reported to be different between diurnal and nocturnal periods [7], we analyzed data during nocturnal and diurnal periods separately. Nocturnal data shorter than 5 hours were excluded from analysis to preserve sufficient data points.

2.2 Detrended Fluctuation Analysis

First, we analyzed the activity data by the "detrended fluctuation analysis" (DFA) [8, 9], as in [7]. The DFA is a method used to analyze temporal correlations of time series by calculating average fluctuations of the data in various scales after removing local trends [9]. The DFA method is defined as follows: One first integrates the physical activity time series. One then divides the time series into "boxes" of length n and performs, in each box, a least-squares polynomial fit to the integrated signal. Next, one calculates in each box the root-mean-square deviations from the regression line. This procedure is repeated for different box sizes (time scales) n. For fractal signals one finds a power-law relation between the average magnitude of the fluctuations $F(n)$ and the number of points n:

$$F(n) \sim n^{\alpha}, \quad (1)$$

where the scaling exponent α quantifies the degree of the correlations. Uncorrelated time series yield $\alpha = 1.5$, while anti-correlations result in $\alpha < 1.5$.

In this study, the box sizes were increased from $n = 4$ to 7 which are equivalent to analyzing fluctuations within 35 min. The $F(n)$ was calculated from diurnal or nocturnal data for each day, and the resultant fluctuation functions were averaged for the entire 12 days. As some recent studies [12, 13] recommend the k-th order polynomial detrending before calculating $F(n)$, we used the 2nd order DFA in this study in order to compare the results with those by alterna-tive approaches outlined below.

2.3 Wavelet Transform Modulus Maxima Method

Many physiological time series, including physical activity, are extremely "patchy" and nonstationary. Thus, abrupt or "singular" changes, such as bursts of physical activity, may not spread over the entire record. Obviously, the DFA method above holds no information on temporal localizations of such singularities.

Muzy et al. [10] proposed so-called "wavelet transform modulus maxima" (WTMM) method to overcome this difficulty. In this method, for the integrated time series of physical activity $f(x)$ (x; time), one first convolves a mother wavelet $\Psi(x)$:

$$T\psi[f](b,a) = \frac{1}{a}\int_{-\infty}^{\infty} \psi\left(\frac{x-b}{a}\right) f(x)dx, \quad (2)$$

where a and b are the scale and the localization of the mother wavelet, respectively. In this study, we used the Gaussian 3rd derivative,

$$\psi(x) = x(3-x^2)e^{-0.5x^2}, \quad (3)$$

as the mother wavelet with the values of $1 \leq a \leq 7$ corresponding to < 35 min. This wavelet has vanishing moments of the 0th, 1st, and 2nd orders:

$$\int_{-\infty}^{\infty} \psi(x)x^q dx = 0, \quad (4)$$

for $q = 0, 1$ and 2. This means that the mean, the linear trend, and the 2nd order polynomial trend of the integrated time series are successfully eliminated as also done by the DFA method.

The next step of Muzy et al.'s approach is to only use a set of points where the wavelet moduli (Eq. 2) take the local maxima, or at the modulus maxima (MM), in evaluating scaling relationships [10]. Here the MM are defined as any point (x_0, a_0) that satisfies $|T\Psi[f](x_0, a_0)| > |T\Psi[f](x, a_0)|$ for all x in the right neighborhood of x_0 and $|T\Psi[f](x_0, a_0)| \geq |T\Psi[f](x, a_0)|$ for all x in the left neighborhood [10], and by these MM one can only pick up characteristic singularities (e.g., activity bursts) as shown in Figure 1. This feature is thought to be important especially for physical activity time series because the bursts of activity are indeed sporadic.

In this study, we only picked up the MM with negative $T\Psi[f]$ (i.e, negative MM or NMM), different from the original method by Muzy et al. [10]. As shown in Figure 1, the integrated physical activity time series have the positive MM or PMM in the middle of activity bursts and the NMM in the middle of resting periods in larger scales and at the onset and cessation of activity bursts in smaller scales. Therefore, the NMM correspond to the interruption of physical activity.

Finally, from the collected NMM, we calculated a sum of the variance of NMM per day (NMM power) for each subject, which corresponds to a "partition function" $Z(a)$ of the 2nd order [10]. From this $Z(a)$, the scaling exponent τ, corresponding to the α in Eq. 1, were calculated as:

$$Z(a) \sim a^{\tau}. \quad (5)$$

The $Z(a)$ was calculated from diurnal or nocturnal data for each day, and the resultant partition functions were averaged for the entire 12 days. Hereafter, we call the modified Muzy et al.'s method in this study as the "wavelet transform negative modulus maxima" (WTNMM) method.

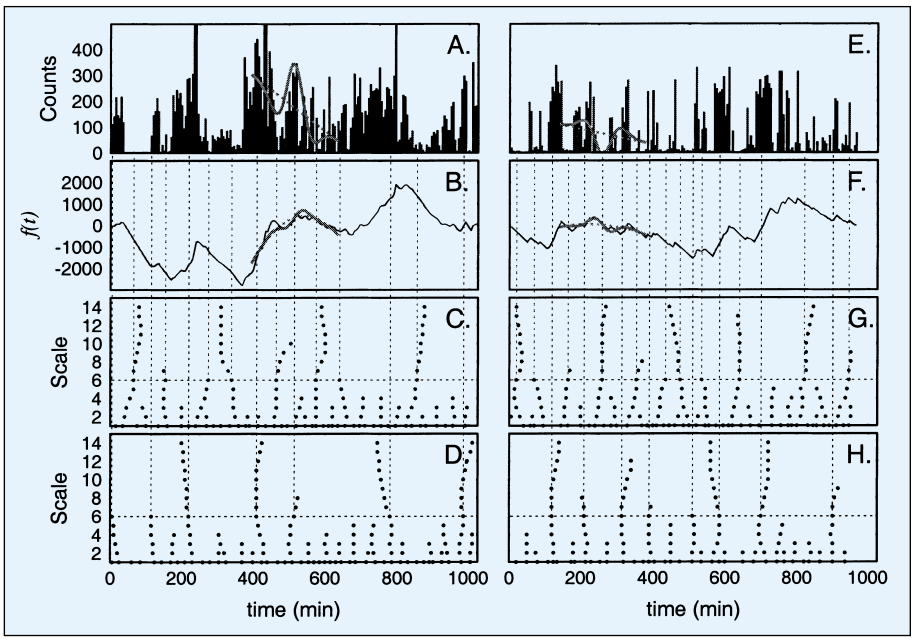

Fig. 1 Diurnal records of physical activity (A and E), the integrated activities (B and F), the locations of NMM of the wavelet transform of the integrated series (C and G), and PMM (D and H) for a healthy subject (A - D) and a patient with CFS (E - H). The Gaussian 2nd and the 3rd derivatives (scale 6 corresponding to 30 min) with the linear and the second order polynomial trends are respectively shown in green on the physical activity records and the integrated series as examples for the PMM (left) and NMM (right). The physical activity and the integrated activities are colored red at the locations of all NMM, while blue for all PMM, with the width of about an hour. The data are colored magenta when the NMM and PMM are overlapped. Note that the NMM are located at the interruption of activities while the PMM detect singularities at activity bursts.

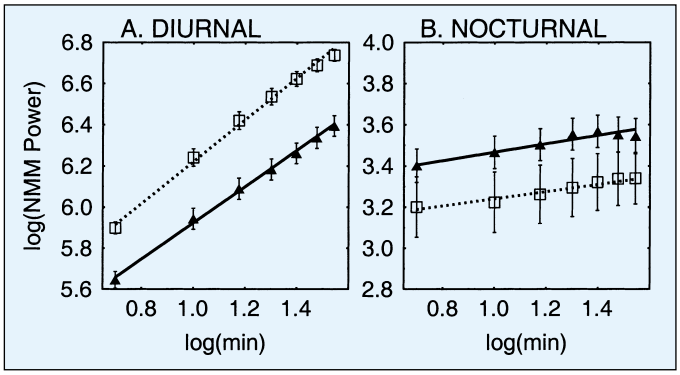

Fig. 2 Temporal correlations of human physical activity by the WTNMM method. The NMM power are plotted in double-logarithmic scales for CFS and CON during diurnal (A) and nocturnal (B) periods. Filled triangles and open squares are the group means for CFS and CON, respectively. Vertical bars represent S.E.M. The regression line for <35 min is shown in each panel. Solid and dashed lines are the regression lines for CFS and CON, respectively. Note that the vertical axes differ for both panels but the ranges are adjusted so that the slopes are comparable between diurnal and nocturnal data.

Table 1 The scaling exponents τ by the WTNMM method and α by the DFA method. Values are means ± S.E.M. *; $p<0.01$ between CFS and CON by the standard t-test.

τ by WTNMM		α by DFA	
CFS (n=10)	CON (n=6)	CFS (n=10)	CON (n=6)
Diurnal			
0.87±0.03*	1.01±0.03	1.45±0.03	1.60±0.07
Nocturnal			
0.20±0.04	0.22±0.03	1.01±0.08	0.92±0.11

3. Results

3.1 Temporal Correlation

Fig. 2 shows the results of the WTNMM method applied to the activity data. Up to scale 7 corresponding to 35 min, the NMM power exhibited straight lines in log-log axes in both CFS and CON. This suggests that physical activity for both CFS and CON have fractal time organization for at least up to 35 min. The NMM power reduced considerably in CFS as compared to CON, in accordance with the decreased magnitude of physical activity reported for these patients [4]. In addition, the slopes of regression, i.e., the scaling exponent τ, seem to be smaller in CFS than in CON especially during diurnal periods. For nocturnal data, the τ was smaller than that for diurnal data both in CFS and CON without the group difference. These results indicate that CFS patients have qualitatively different physical activity at the interruption of activity bursts compared to healthy controls during diurnal periods.

3.2 Sensitivity to Identify CFS Patients

Table 1 summarizes the results for the scaling exponents τ and α. The diurnal τ by the WTNMM method for CFS was significantly smaller than that for healthy controls. In contrast, there was no significant difference between groups during nocturnal periods. The results of the DFA method were compatible with the previous result by Amaral et al. [7] in that the diurnal α was higher than the nocturnal α. However, the α values could not locate any significant difference between CFS and CON. We also examined an ability of the original WTMM method [10] and the singularities of PMM to discriminate the patients from healthy controls, but these methods were also insensitive to the group differences (data not shown). These results clearly indicate the decreased power-law, fractal correlations in diurnal physical activity time series in patients with CFS and that such differences can only be identified by the WTNMM method picking

up the singularities at the interruption of activity bursts.

4. Discussion

A key finding of this study is that there was a qualitative difference in diurnal physical activity in CFS patients and healthy control subjects. This difference was not seen during nocturnal periods. To our knowledge, this is the first study to report the alteration in temporal structure of physical activity not only for CFS but also for any psychiatric and/or psychosomatic disorders having abnormalities in physical activity. The fractal temporal correlations were preserved in the CFS data, but the characteristic exponents τ were significantly smaller, leading to a shorter temporal correlation or stronger singularities in the middle of resting periods. It thus appears as if very inactive CFS patients in this study are likely to have, in a statistical sense, abrupt interruptions of physical activity, presumably due to their exaggerated fatigue. In contrast, for healthy controls, the demands of daily life might hinder the development of such patterns, leading to weaker singularities and larger values of τ. Hence, it is plausible that our finding of decreased fractal correlations in diurnal activity levels of CFS patients provides a new window into the study of disorders associated with abnormal patterns of physical activity. Although CFS resembles depression, empirical data indicated that the two processes are not the same [14]. Nonetheless, the similarities suggest that the methods used here might be useful in providing a marker for depression as well as for other disorders producing reductions in activity.

In this study, we also found that the WTNMM method was the most sensitive in discriminating very inactive CFS patients from healthy controls. This suggests that, in physical activity time series, the positive and the negative MM could correspond to substantially different phases of patients' activity and one may have to analyze their singularities separately. Whether this method would also be useful for other types of time series will be studied further.

Acknowledgement
We thank S. B. Lowen, M. H. Teicher, and H. E. Stanley for stimulating discussions. Y.Y. acknowledges a MECSST Grant-in-Aid for Scientific Research and Japan Science and Technology Corporation.

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