Method for Detecting Quantitative Differences in the Parameters of Involuntary Effort Fluctuations in Healthy Volunteers and Patients with Parkinson's Syndrome

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny,* Vol. 146, No. 10, pp. 477-480, October, 2008
Original article submitted December 5, 2007

The aim of the study was to detect quantitative differences in the parameters of involuntary effort fluctuations in healthy volunteers and patients with Parkinson's syndrome. Using a mathematical model, the process of isometric effort maintenance was separated into rapid (involuntary) and slow (voluntary) constituents. Significant differences were detected for the attenuation coefficient of fluctuations in the involuntary constituent, but not for the frequency.

Key Words: *isometric effort; model; fluctuations; parkinsonism; quantitative differences*

Detection of quantitative differences in the process of balance maintenance in health and disease is of crucial importance for the treatment of motor disorders associated with Parkinson's syndrome. As a rule, this process is evaluated by analyzing the frequency spectrum of fluctuations emerging during maintenance of isometric effort of human hand [1,4]. The developing disease is attributed to synchronization of the motor units fluctuations, which are normally assumed to be desynchronized [3,6]. Treatment with antiparkinsonism agents modifies the high-frequency band virtually without modulating the frequencies below 10 Hz [2,5]. However, the frequencies of 5-10 Hz are essential in various forms of Parkinson's tremor. Therefore, detailed analysis of not only frequency, but of other parameters of fluctuations is an important problem.

The process of maintenance of human hand isometric effort has two constituents. They include continuous activation of muscular effort and continuous visual observation of the permanent deviations of the checkpoint on the monitor by the examined subject. Hence, isometric effort during this process leads to two parallel events. One event are permanent fluctuations, realized by means of muscular efforts, the other is continuous regulation of these fluctuations. Hence, two mechanisms are involved in this process. One creates continuous deviations from the checkpoint on the monitor, while the other regulates the process of their stabilization. We refer these fluctuations to the involuntary constituent of isometric effort, while the process of these fluctuations regulation is the voluntary constituent.

The aim of our study is to develop a method for separating the process of isometric effort maintenance into voluntary and involuntary constituents and detect quantitative differences in the parameters of involuntary effort fluctuations in healthy volunteers and patients with Parkinson's syndrome.

MATERIALS AND METHODS

Experiments were carried out in 11 healthy volunteers (31-45 years) and 11 patients with Parkinson's

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syndrome (47-59 years). Five of these patients had symptomatic and 6 rigid akinetic forms of parkinsonism. No drugs were used 24 h before experiment.

Isometric effort, maintained by the examined subject by two hands simultaneously, was recorded. The examined subject was sitting and pressing the pickups by 4 fingers of each hand for 30 sec. The strength of left and right hand efforts presented on the monitor by deviations from the checkpoints. The frequency of data registration was 100 Hz; two series with 3000 points (reference points) for right and left hands of each examined subject were analyzed.

A window was selected on the recorded trajectory, its beginning coincided with the beginning of trajectory, its length being 3 reference points. The trajectory within the window was approximated by the following model:

$$f(t)=(r\sin\omega t+s\cos\omega t)\exp(-\lambda t)+a+bt+ct^2, \quad (1)$$

where ω and λ are cyclic frequency and attenuation coefficient.

Coefficient of correlation between the model curve and experimental trajectory was calculated. Then the next window of the same length was analyzed, shifted by one reference point along the registered trajectory, and the procedure was repeated. The mean (for all windows) coefficient of correlations was calculated. Then the length of the window was increased by one reference point, and the procedure was repeated until the length of the window reached 11 reference points. The length of the window with the maximum coefficient of correlations was chosen for the optimal length.

In order to determine the parameters of model **(1)**, we took into consideration the fact that model **(1)** was a solution of the differential equation:

$$\ddot{f}(t)-2l\dot{f}(t)+(\lambda^2+\omega^2)f(t)=H+Et+Kt^2, \quad (2)$$

where $H=2c-2\lambda b+a(\lambda^2+\omega^2)$; $E=-4\lambda c+b(\lambda^2+\omega^2)$; $K=(\lambda^2+\omega^2)c$.

Hence, in order to determine the parameters, we had to calculate the values of $\dot{f}(t)$ and $\ddot{f}(t)$ functions, for which the trajectory was approximated by a cubical polynomial within each window and this polynomial coefficients were found, from which $\dot{f}(t)$ and $\ddot{f}(t)$ values were found. A system of the following equations was then solved:

$$\begin{cases} \ddot{f}(t_i)=2\lambda f(t_i)-(\lambda^2-\omega^2) \\ f(t_i)-H-Et_i-Kt_i^2=0, \end{cases} \quad (3)$$

where i=1, ..., n, (n is number of windows), for 2λ, $\lambda^2+\omega^2$, H, E, K values. Then the λ, ω, a, b, and c parameters were calculated. The r and s values were found as solutions of equation **(1)**, presented as $f(t)-a-bt-ct^2=(r\sin\omega t+s\cos\omega t)\exp(-\lambda t)$.

RESULTS

The coefficient of correlation between the model curve and experimental trajectory was at least 0.98 for all examined subjects, this indicating high precision of approximation of the registered trajectory by model **(1)** in the selected window.

The trajectory of recorded isometric effort and its two constituents are presented in Fig. 1. The

TABLE 1. Mean Frequencies ($f=2\pi/\omega$) and Attenuation Coefficients (λ) for the Involuntary Constituent of Registered Efforts of Right and Left Hands in Healthy Volunteers and Patients with Parkinson's Disease

No.	Volunteers		Patients		Volunteers		Patients	
	left hand	right hand	left hand	right hand	left hand	right hand	left hand	right hand
	f (Hz)	f (Hz)	f (Hz)	f (Hz)	λ	λ	λ	λ
1	8.8	8.6	9.9	9.7	18.1	37.4	15.5	10.5
2	8.9	8.9	10.1	10.2	22.2	22.1	17.3	17.6
3	9.7	13.4	11.5	14.0	23.1	20.2	25.2	11.4
4	10.5	9.5	9.7	10.1	17.1	17.3	21.4	11.3
5	10.6	10.4	8.1	8.1	27.5	23.1	15.3	12.3
6	12.0	11.7	10.3	9.6	18.1	26.4	3.8	4.2
7	10.0	11.0	7.5	10.8	36.4	21.1	15.1	13.5
8	10.3	11.7	10.8	11.4	20.1	17.5	14.4	23.1
9	13.0	11.7	8.9	9.9	23.2	29.5	14.2	15.2
10	10.7	10.5	8.9	10.9	19.1	18.2	10.9	9.7
11	13.8	12.4	8.7	8.2	25.9	18.4	12.3	15.1
Mean	10.8	10.9	9.5	10.3	22.5	22.5	14.6	12.7

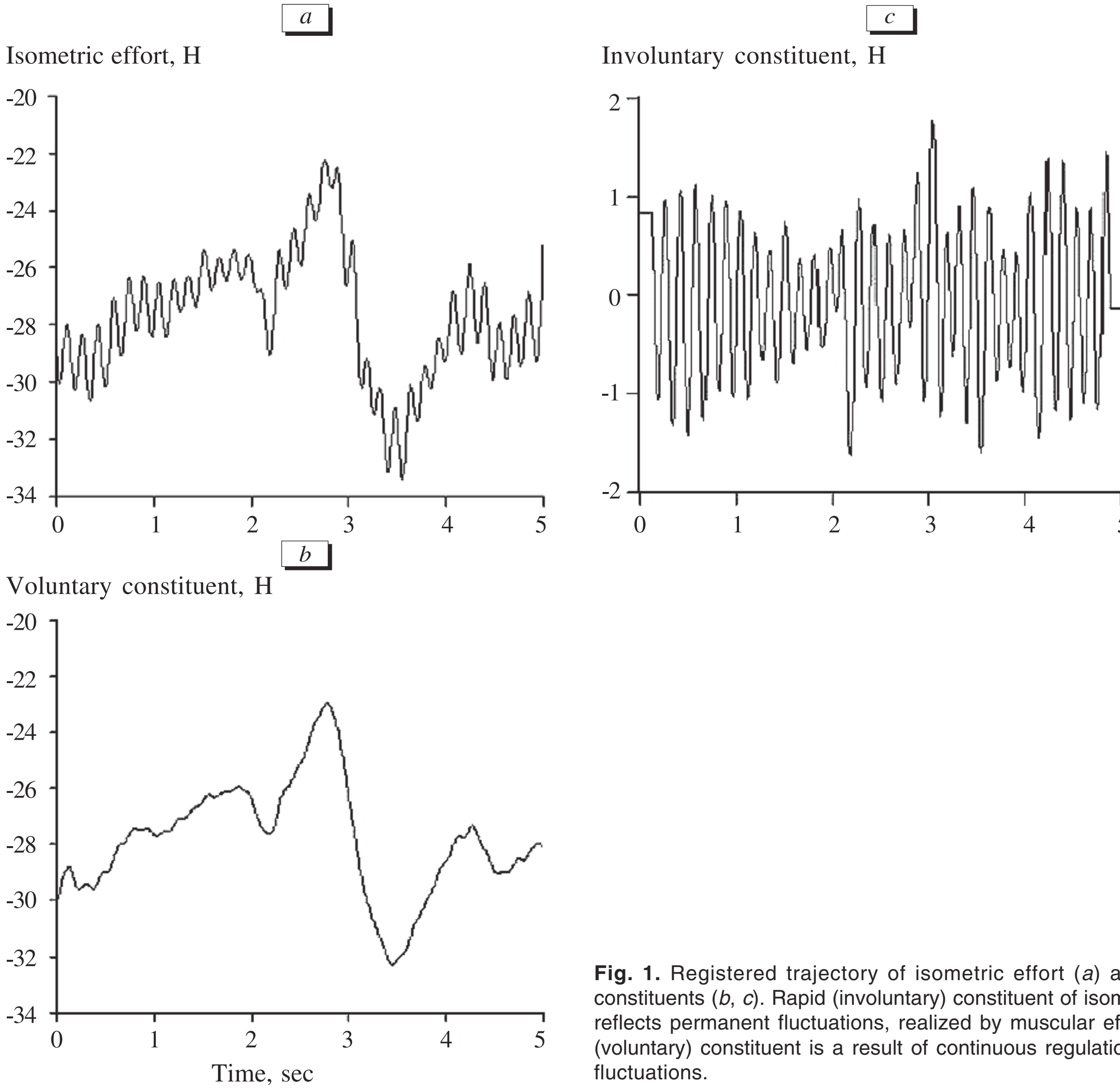

Fig. 1. Registered trajectory of isometric effort (*a*) and its two constituents (*b*, *c*). Rapid (involuntary) constituent of isometric effort reflects permanent fluctuations, realized by muscular efforts. Slow (voluntary) constituent is a result of continuous regulation of these fluctuations.

rapid (involuntary) constituent of isometric effort reflects the involuntary fluctuations realized by muscular efforts. The slow (voluntary) constituent is a result of continuous regulation of these fluctuations. The time pattern of the rapid constituent is close to nonstationary quasiperiodical fluctuations. By contrast, the "voluntary" regulation rules out the clear-cut time pattern of the slow constituent.

This model makes it possible to detect quantitative differences in the parameters of fluctuations of involuntary effort in healthy volunteers and patients with Parkinson's disease.

The mean values of frequency (f=2π/ω) and attenuation coefficient (λ) in 11 normal subjects and 11 patients are presented in Table 1. The differences in the means for parameters f and λ were evaluated using Student's t test. The hypothesis on the equality of these means was verified in patients and normal subjects. The values of significance for differences in the mean frequencies in patients and normal subjects were 0.018 (for left hand) and 0.176 (for right hand). Hence, for the left hand the hypothesis of equality of the mean frequencies in patients and normal subjects is rejected at the 5% level of significance, while for the right hand this hypothesis is confirmed at the same level of significance. The significance of differences in the mean coefficient of attenuation for patients and normal subjects is 0.0002 (for left hand) and 0.0016 (for right hand), that is, the hypothesis of equality of the mean coefficients of attenuation in patients and normal subjects is rejected at less than 1% level of significance. Therefore, essential differences in the isometric effort trajectory in healthy volunteers and patients with Parkinson's syndrome are observed only for the involuntary effort coefficient of attenuation. Hence, the proposed method detects the differences in the parameters of nonstationary processes and can be used for evaluating the treatment efficiency.

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