PHYSIOLOGY

Analysis of Differences between Physiological and Pathological Tremor of Human Fingers

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The study tried to reveal the differences between physiological and pathological tremor appearing during maintenance of isometric force in healthy individual and parkinsonian patients with tremor. Six-level wavelet expansion was used presenting the tremor as a sum of smoothed (slow) component and high-frequency detailed components of 6 expansion levels. The differences in the high-frequency components were assessed by calculating the energetic parameters in the power spectrum of these components. These parameters make it possible not only to reliably distinguish the energetic spectra of the detail components of the physiological and pathological tremor, but also to correlate changes in patient state caused by drug treatment of parkinsonian trembling with the decrease in these parameters.

Key Words: *tremor; parkinsonism; wavelet expansion; energetic parameters*

Tremor, involuntary trembling movements, can accompany any intentional movements of humans and can be related to neural activity both in the central structures of the motor system and at the segmental level with involvement of the proprioceptive reflex pathways [8]. Physiological tremor is characterized by frequency range of 8-12 Hz and low amplitude virtually invisible by naked eye [5]. Isometric efforts, stress, and fatigue augment the tremor amplitude due to increased synchronization of neural activity at all levels of the locomotor system [6]. Elastic load developed by the fingers of a healthy subject needs careful control of their position. Under these conditions, 10-Hz oscillations are accompanied by trembling at 20 and 40 Hz [9]. The appearance of these high frequencies is usually explained by the involvement of sensory information processing. Studies of parkinsonian tremor showed that different frequencies correspond to specific levels of the motor regulation. For instance, parkinsonian patients are characterized by pathological tremor at 3-6 Hz and the lack of the frequencies above 15 Hz [4]. Antiparkinsonian preparations alleviating parkinsonian symptoms induce 40-Hz tremor, which disappears after withdrawal of these drugs. This observation corroborates the view that high-frequency neural activity plays a certain role in the regulation of movements, and this activity is disturbed during parkinsonism [9]. Tremor during maintenance of isometric effort of an arm (without finger movement) in healthy and parkinsonian individuals differs by amplitude, but little differs by frequency within the range of 5-12 Hz. This peculiarity underlies the problems of differentiation the frequency spectra. Assessment of energy spectrum or power spectrum for a non-stationary process (*e.g.* tremor) is difficult due to blurriness of their frequency bands. Therefore, it is difficult to compare such spectra in the search of the peculiar features related to different experimental conditions.

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Our aim was to reveal the differences in kinetic tremor appearing during maintenance the muscular effort of an arm in healthy subjects and in patients with Parkinson's disease tremor on the basis of tremor power spectrum analysis.

MATERIALS AND METHODS

Healthy subjects (n=9) and patients with primary parkinsonism of the second degree according to Hoehn–Yahr scale [7] (bilateral manifestations of tremor and akinesia without signs of balance problems, n=9) aging 45-50 years were examined. The examinees sat at the table in front of the monitor and pressed the special platforms with fingers of stretched arms. The platforms were equipped with pressure transducers, which converted pressure into electrical signal. Sufficiently high rigidity of the platforms provided recording of the muscle effort under isometric conditions without appreciable motion of the fingers. The examinees were instructed to maintain the maximum force with four fingers in vertical direction downwards for 30 sec. The forces developed by the right and left hand were recorded individually. On the day of examination, parkinsonian patients received no medication before recording. The patients usually compensated dopamine deficiency three times a day with antiparkinsonian preparation madopar containing levodopa and benserazide (dopadecarboxylase inhibitor) in doses of 200 mg and 50 mg, respectively. The recorded plot of isometric force contained a slow trend and a fast involuntary component (tremor). The latter was extracted from this plot using a "wden" procedure available in MATLAB software. To characterize the difference between physiological and pathological tremor, we used wavelet transform [2] and related MATLAB procedures that expands tremor $\{x(t_i)\}^N_{i=1}$ over the set of copies of prototype function (mother wavelet), which are scaled to a certain degree and shifted along the time axis by some distance. In this way, discrete transform of the initial signal is presented at the m-level of expansion as a superposition of wavelets and scaling functions. The inverse wavelet transformation presents the tremor as the sum of the smoothed component of the last level (A_m) and the detail components of all levels (D_m, …, D_1): $x(t_i)=A_m(t_i)+D_m(t_i)+ \dots +D_1(t_i)$, where $A_m(t_i)$ is a rough approximation of the original tremor at the m-level of expansion, while $D_1(t_i)$, …, $D_m(t_i)$ are the small-scale details obtained on the first, … and m-level of expansion. Here, $D_1(t_i)$ characterizes the detail component of the highest frequency.

In this study, we used Daubechies wavelet db_4 as the mother wavelet with the central frequency of f_r=0.71 Hz. The frequency corresponding to j-level expansion was calculated according to the formula:

$$Fr_j=\frac{f_r f_s}{2^j},\ j=0,\ \dots,\ 5,$$

where f_S=50 Hz is sampling rate. At each level of expansion, the frequencies greater than Fr were filtered out. Thus, the first level (j=0) of expansion included frequencies ≤35.5 Hz, while the frequencies at the last (sixth, j=5) level were below 1.6 Hz. The resulted components of the tremor plot were analyzed using previously developed method assessing the parameters of signal power spectrum [3].

The power spectrum of the signal equals to $E(f)=|\int x(t)e^{-2\pi ift}dt|^2$. The integral $E=\int_{f_1}^{f_2}(f)df$ describes accumulation of the energy within the frequency band between f_1 and f_2 boundaries. The following values were used as the energetic parameters of the power spectrum:

$$h_1=\frac{C}{(f_2-f_1)f_{\max}},\ h_2=\frac{E_{\max}}{f_{\max}},\ \textbf{(1)}$$

Here E_{max} is maximum of the power spectrum, f_{max} is the frequency corresponding to this maximum, C is the maximum of energy accumulation, and (f_1, f_2) is the frequency interval with power spectrum >5% of maximum value (the power spectrum outside this band is considered as noise).

RESULTS

In all healthy examinees, the amplitude of the fast involuntary component of isometric force (tremor) was 2-fold lower than in parkinsonian patients with tremor. The frequencies in both groups did not visually differ. This observation agrees with the data previously obtained in healthy subjects and in the patients with drug-induced parkinsonian syndrome. They were examined with a mathematical model simulating maintenance of muscular effort, which demonstrated that significant difference between both groups can be observed not in the frequency, but in the tremor attenuation coefficient [1]. In 1.5 h after administration of antiparkinsonian preparation madopar in a usual dose of 200/50 mg (levodopa/benserazide), the tremor amplitude decreased to a level characteristic of healthy subjects, while the frequency change cannot be observed visually. The 6-level wavelet expansion presented the tremor as the sum of smoothed component of the last (sixth) level A_6 and the details of all levels (D_6, …, D_1). At the first, second, and the subsequent levels, the frequencies higher than 35.5 Hz, 17.7 Hz, *etc*. were respectively filtered off. An example of wavelet expansion of physiological tremor is shown in Fig. 1.

Power spectra of the detail component D_1, D_2, and D_3 of tremor plot are shown in Fig. 2. The presence of

separated peaks in the wavelet power spectra of parkinsonian patients exemplifies a well-known phenomenon of synchronization of motor fiber discharges, while in a healthy organism such discharges are asynchronous [10]. The synchronization effect was observed at all levels of expansion. Madopar insignificantly modified the power spectra (Fig. 2) in the high-frequency range and did not change the spectrum at the frequencies below 10 Hz that are most important for the patients.

The maxima of power spectra correspond to the levels of accumulated energy. The last (maximum) accumulation level was taken for C constant used in formula (**1**) to calculate h_1.

Table 1 shows the h_1/h_2 ratios of mean energetic parameters of power spectra at various levels of wavelet expansion. At expansion level 2, the mean values of h_1 for maximum muscular effort of the left and right hands of parkinsonian patients surpassed the corresponding values of healthy subjects by 80 and 95 times, while at the level 6, the respective overshoots were only 1.9- and 3.1-fold. The differences in h_2 energetic parameter were less pronounced. For example, at the expansion level 2, the mean values of h_1 for maximum muscular effort of the left and right hand of parkinsonian patients surpassed the corresponding values of the healthy subjects by only 27 and 22 times, while on the level 6, the respective overshoots were mere 2 times for any hand.

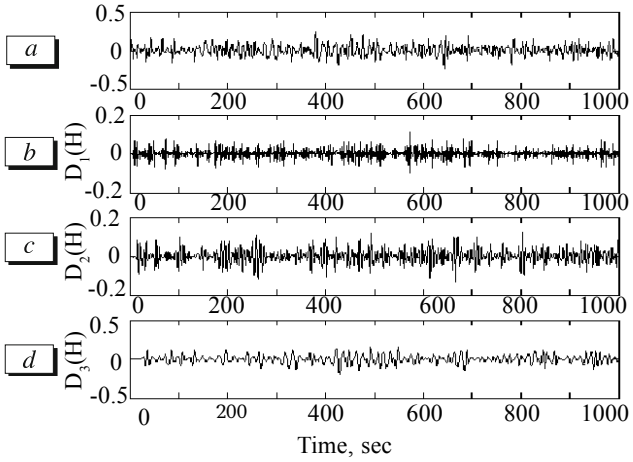

Fig. 1. An example of wavelet expansion of physiological tremor. Shown are the original plot (*a*) and the first three detail components D_1 (*b*), D_2 (*c*), and D_3 (*d*). D_1 is the highest frequency component.

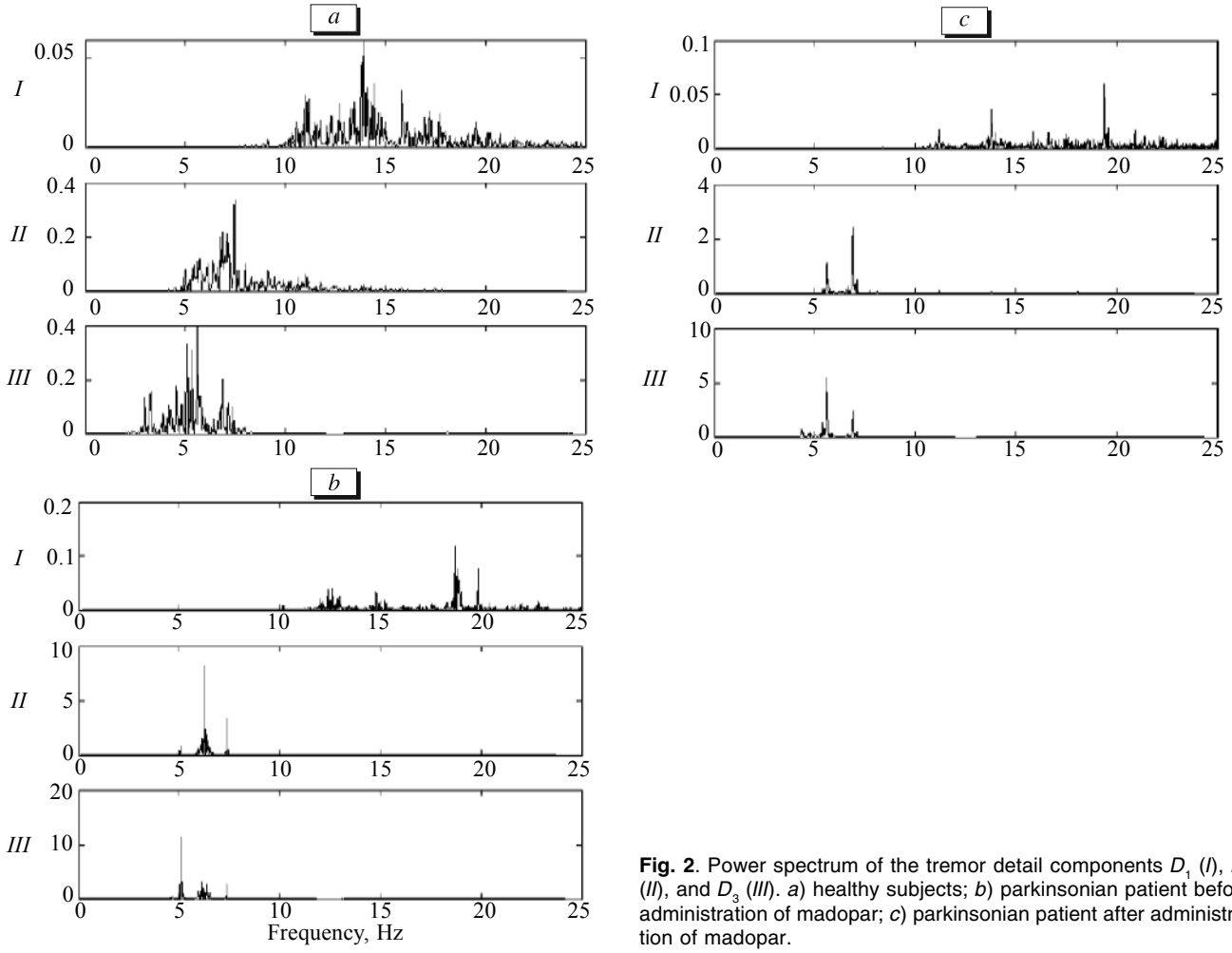

Fig. 2. Power spectrum of the tremor detail components D_1 (*I*), D_2 (*II*), and D_3 (*III*). *a*) healthy subjects; *b*) parkinsonian patient before administration of madopar; *c*) parkinsonian patient after administration of madopar.

TABLE 1. Ratios of the Mean Values of Energetic Parameters h_1 and h_2 of Tremor Power Spectra at Various Levels of Wavelet Expansion (n=9)

Arm, parameter		Expansion level				
		2	3	4	5	6
Left arm	h_1 (park)/h_1 (hl)	80.93±7.00	16.95±1.70	10.78±1.00	7.85±0.70	1.90±0.09
	h_1 (park+madopar)/h_1 (hl)	60.73±50	11.95±0.70	8.35±0.40	6.47±0.30	1.17±0.08
	h_2 (park)/h_2 (hl)	27.13±1.50	12.19±0.80	10.5±0.7	7.05±0.40	2.12±0.10
	h_2 (park+madopar)/h_2 (hl)	10.91±0.80	6.46±0.40	4.97±0.30	3.47±0.20	1.49±0.08
Right arm	h_1 (park)/h_1 (hl)	95.71±7.00	29.32±1.70	17.83±1.00	9.79±0.70	3.12±0.09
	h_1 (park+madopar)/h_1 (hl)	72.32±5.00	13.71±0.70	9.51±0.40	6.92±0.30	1.28±0.08
	h_2 (park)/h_2 (hl)	22.72±1.40	9.74±0.60	8.41±0.60	5.90±0.30	2.74±0.10
	h_2 (park+madopar)/h_2 (hl)	11.36±0.70	6.49±0.30	5.48±0.30	4.08±0.20	1.98±0.20

Note. Symbols *h* (park) and *h* (park+madopar) denote the corresponding energetic parameters for parkinsonian patient before and after administration of madopar; symbol *h* (hl) denote these parameters for healthy subjects.

In 1.5 hour after madopar administration, the differences between the mean values of h_1 and h_2 in healthy subjects and parkinsonian patients decreased at all expansion levels. At the level 2, h_1 parameter for left and right hand differed by 60 and 72 times, respectively, while the differences for h_2 parameters were 11-fold for both hands. At the last expansion level, the mean values of h_1 in healthy subjects and parkinsonian patients did not differ, while the differences in parameter h_2 for the left and right hands were 1.5 and 2 times, respectively. This observation attests to the fact that 1.5 h after administration of the drug, which compensates dopamine deficiency in the basal ganglia, the kinetic tremor appearing during the effort to maintain the isometric force by the parkinsonian patients with tremor, insignificantly differed by power spectrum parameters from that of normal physiological tremor. Thus, the analyzed energetic parameters of wavelet expansion "keenly feel" the changes in the human state and can serve as the criteria, which differentiate the power spectra of the detail components in the cases when the frequency parameters of pre- and postmedication tremor are virtually identical.

REFERENCES

1. Ya. A. Bedrov, O. E. Dick, S. P. Romanov, and A. D. Nozdrachev, *Byull. Eksp. Biol. Med.,* **146**, No. 10, 477-480 (2008).
2. S. Malla, *Wavelets in Signal Processing* [Russian translation], Moscow (2005).
3. V. M. Musalimov, O. E. Dick, and A. E. Tyurin, *Izv. Vuz. Priborostroen.,* **52**, No. 5, 10-15 (2009).
4. P. Brown, D. M. Corcos, and J. C. Rothwell, *Brain,* **120**, Pt. 3, 401-408 *(*1997).
5. R. Elble, *Neurology,* **36**, No. 2, 225-231 (1986).
6. K. E. Hagbarth and R. R. Young, *Brain,* **102**, No. 3, 509-526 (1979).
7. M. M. Hoehn and M. D. Yahr, *Neurology,* **17**, No. 5, 427-442 (1967).
8. J. H. McAuley and C. D. Marsden , *Brain,* **123**, Pt. 8, 1545-1567 (2000).
9. J. H. McAuley, J. C. Rothwell, and C. D. Marsden, *Exp. Brain Res.,* **114**, No. 3, 525-541 (1997).
10. A. Prochazka and P. S. Trend, *J. Physiol.,* **402,** 421-442 (1998).