METHODS

Study of Magnetic Field of the Brain in Parkinson's Disease

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The magnetic field of the brain in parkinsonism was studied. Magnetic encephalography data were analyzed by a comprehensive spectral method. Sources of magnetic activity of the brain were simulated by punctate current dipoles. Based on the results of classification, we detected the pattern of high magnetic activity; this opens new vistas for the diagnosis and treatment of Parkinson's disease.

Key Words: *neurodegenerative diseases; magnetic encephalography; location of magnetic field source*

Parkinson's disease is one of the most prevalent neurodegenerative diseases all over the world, leading to motor disorders (muscle rigidity, tremor, bradykinesia, akinesia, balance disorders), depression, dissemination of attention, amnesia, and dementia [4].

The diagnosis of parkinsonism is very difficult, particularly at the early stages. Due to creation of new sensitive methods, based on measurements of electric potentials (electroencephalography — EEG) and magnetic fields (magnetic encephalography — MEG), it is possible to identify damaged brain sites, which is important for the diagnosis of early stages of the disease and evaluation of the treatment results.

Magnetic encephalography is a method for measurement and visualization of magnetic fields emerging as a result of electric activity of the brain. This method is used for studies of the functional regions and for diagnosis of various diseases. This rapid completely noninvasive technology is useful in studies of the processes running inside the brain cortex. In contrast to widely used EEG [3], MEG precisely locates the source of magnetic field [2]. This explains the main sphere of application of the method: recognition and recording of pathologic activity zones in neurodegenerative diseases, for example, in Parkinson's disease [5].

We developed a spectral method for classification of MEG data, location of magnetic field sources, and studied various types of activity in parkinsonism.

MATERIALS AND METHODS

Measurements of magnetic fields of the brain were carried out at New York Medical School. Fourteen patients with parkinsonism, aged 50-70 years, gave written consent to participation in the study. The study was carried out on a Magnes 2500 WH encephalometer.

One of the main components of MEG device is a superconducting quantum interference pickup (a closed semiconductor circle with a Josephson's contact in one or two places). These contacts work only at the superconduction temperatures, which is fraught with technological difficulties, as only work

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at low temperatures, when the thermal murmur of the pickup is reduced, allows the creation od the most sensitive devices [1]. However the environmental magnetic fields (permanent magnetic field of the Earth, 10^{10}, and the basal field of a city, 10^7-10^8) and human body fields (lungs: 10^6, digestive system: 10^5; cardiogram: 10^4) are much more potent than the magnetic field of the brain (evoked activity of the brain stem cells is 1). During the study the patients were placed into a noise-proof experimental room shielded from the external magnetic fields.

The measured signal represented a spatial and time structure: a 148-dimensional vector of measurements in 148 points on the head surface, unfolded in a time series with 500 Hz frequency of pickup scanning.

Data processing included distinguishing of sites of digital biomagnetic signal, characterizing various types of activity, and location of sites of high biomagnetic activity. Cluster analysis of the data was carried out using Statistica 7.0 software. Sites of high biomagnetic activity of the brain were located using MRIAN software (Institute of Mathematical Problems of Biology) [2].

Analysis of MEG records from patients suffering from Parkinson's disease showed typical spontaneous switch-over between abnormal and normal activities, caused by activation and deactivation of stimulation areas in the brain [2,3,7]. A comprehensive method is suggested for classification of the signal activity. It consists of 5 stages (Fig. 1). One of the most important stages is location of the magnetic field source.

Sources of magnetic activity of the brain are simulated by punctate current dipoles. Each dipole of this kind is characterized by two vectors: r_0 radius vector of dipole (dipole position) and Q vector, presetting the direction and strength of the dipole (dipole moment). The equation for a magnetic field pickup in point r with vector n is as follows [6]:

$$B(r_0, Q)= \frac{\mu_0}{4\pi F^2}((F(Q\times r_0)-(Q\times r_0, \mathrm{r})\nabla F), n),$$

where $F=a(ar+r^2-(r_0, r)$, $\nabla F=(a^2r^{-1}+a^{-1}(a, r)+2a+2r)\mathrm{r}-(a+2r+a^{-1}(a, r))r_0$, $a=r-r_0$, $a=|a|$, $r=|r|$, $|n|=1$, $\mu_0=4\pi\times10^{-7}$, r_0 is dipole vector radius. The current dipole is presented as the current density function:

$$J(r)=Q\delta(r-r_0),$$

where $\delta(r)$ is Diraque's function.

The inverse task of MEG is to find the r_0 and Q parameters, minimizing the error function.

This problem is solved by the method of searching for the local minimum of the function of several variables (by Nelder—Mid's simplex method).

Calculations were carried out using the resources of Interdepartmental Supercomputer Center of the Russian Academy of Sciences.

RESULTS

Classification of the signal type was carried out using our comprehensive method with consideration for the spectral characteristics of the signal. Four signal types were distinguished (A, B, C, D).

The solution of the inverse problem is presented for each moment in time as the current dipole with a variable moment. The sources of biomagnetic activity for moments when type A signal is observed are located in the cerebellum, for signal B they are located in the cerebellum and brain stem, and for signal C in the brain stem (substantia nigra). For moments during which signal D is observed, the sources of biomagnetic activity are located mainly in the cerebral cortex.

A pattern of high magnetic activity was obtained by the results of classification (Fig. 2). This opens new vistas for the diagnosis of Parkinson's disease.

A method for classification of the magnetic signal in Parkinson's disease has been developed (Fig. 1). It consists of 5 steps: expansion by spherical functions, choice of the most informative coeffi-

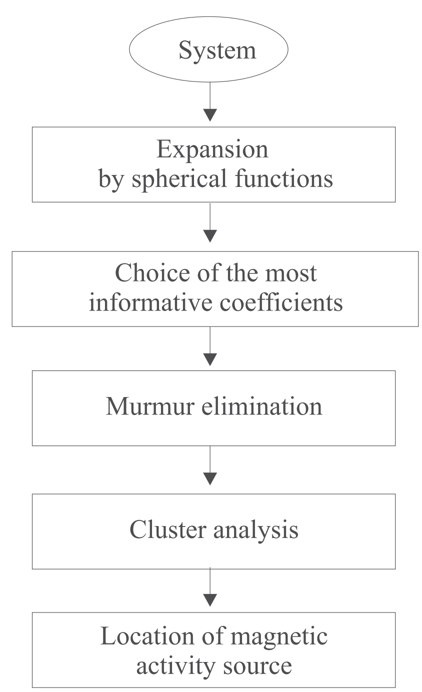

Fig. 1. Spectral method for classification of magnetic signals.

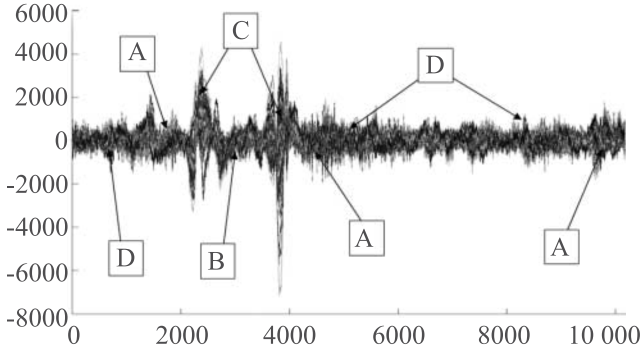

Fig. 2. Fragment of magnetic encephalogram: magnetic field type during a respective moment. Abscissa: time points (1 time period is equal to 1/500 sec); ordinate: magnetic field values (in nT). Source is located: for signal A in the cerebellum, for signal B in the cerebellum and brain stem, for signal C in substantia nigra, and for signal D in the brain cortex.

cients, murmur elimination, cluster analysis of moments of time, location of the source of magnetic activity by the results of cluster analysis. The MEG data were obtained in the spherical coordinate system as a series by orthonormed spherical functions:

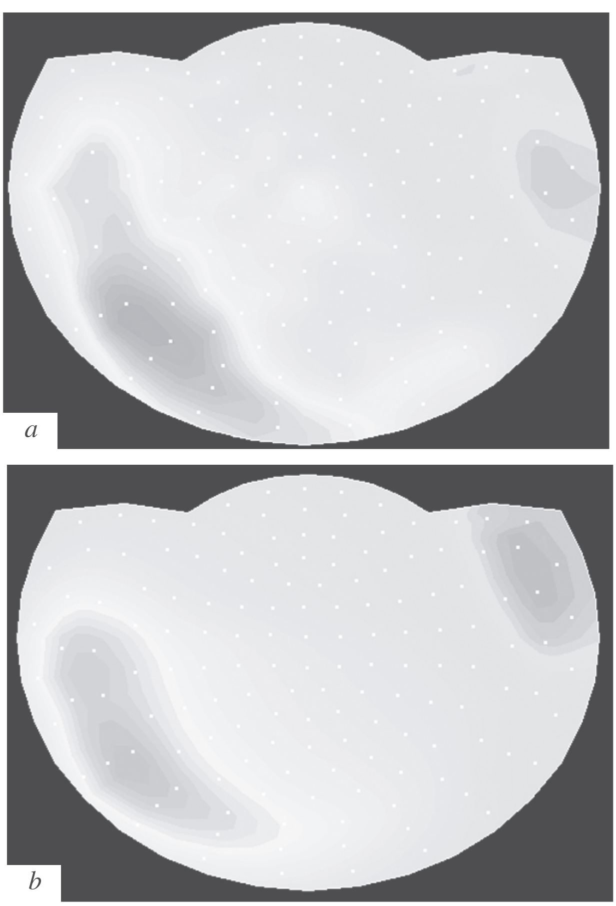

Fig. 3. Distribution of magnetic field on the examined subject's head surface. *a*) initial magnetic field; *b*) magnetic field of located source. The intensity of magnetic field is expressed using a temperature scale.

$$Y^m{}_1(\theta,\ \phi)= \frac{1}{2\pi} P^{|m|}{}_1(\sin\theta)e^{im\phi}.$$

Accordingly, the initial function $f(\theta,\ \phi)$ is determined by the formula:

$$f(\theta,\ \phi)= \sum_{1=0}^{n} \sum_{m=-1}^{1} a_{1m}Y_{1m}(\theta,\ \phi),$$

where expansion coefficients are

$$a_{1m}=\int_0^{2\pi}\int_0^{\pi} f(\theta,\ \phi)Y_{im}(\theta,\ \phi)\sin\theta d\theta d\phi.$$

The requirement of the mathematical expectation to dispersion maximum proportion is regarded as a test for choice of expansion coefficients:

$$\mathrm{IN}=\mathrm{m}_{i \bullet\in[0.35]} \frac{E_i}{D_i}.$$

Use of the method of transition from spatial-and-time recording of MEG to spectral presentation appreciably reduced the scope of data processed and improved the accuracy of calculations. This approach essentially improved the accuracy of the inverse problem solution and provided the optimal accuracy of location of the sources, equal to 2-5 mm (Fig. 3).

Hence, our results can be used for early diagnosis of Parkinson's disease, for planning of surgical interventions, and for evaluation of treatment efficiency.

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