World Academy of Science, Engineering and Technology
International Journal of Medical and Health Sciences
Vol:5, No:2, 2011

A Chaotic Study on Tremor Behavior of Parkinsonian Patients under Deep Brain Stimulation

M. Sadeghi, A.H. Jafari, and S.M.P. Firoozabadi

***Abstract*—**Deep Brain Stimulation or DBS is a surgical treatment for Parkinson's Disease with three stimulation parameters: frequency, pulse width, and voltage. The parameters should be selected appropriately to achieve effective treatment. This selection now, performs clinically. The aim of this research is to study chaotic behavior of recorded tremor of patients under DBS in order to present a computational method to recognize stimulation optimum voltage. We obtained some chaotic features of tremor signal, and discovered embedding space of it has an attractor, and its largest Lyapunov exponent is positive, which show tremor signal has chaotic behavior, also we found out, in optimal voltage, entropy and embedding space variance of tremor signal have minimum values in comparison with other voltages. These differences can help neurologists recognize optimal voltage numerically, which leads to reduce patients' role and discomfort in optimizing stimulation parameters and to do treatment with high accuracy.

***Keywords*—**Chaos, Deep Brain Stimulation, Parkinson's Disease, Stimulation Parameters, tremor.

I. Introduction

PARKINSON'S disease is the most common movement disorder which is seen in old people [1]. It is assumed by most neurologists that the reduction of dopamine neurotransmitter at some parts of Basal Ganglia causes this disease [2]. Tremor is the most important symptom of this disease, and results in a rhythmic oscillation with a frequency of 4-6 Hz [3]. Usually prescribed Levodopa, a combination of dopamine, is the first treatment for this disease [4]. When it releases neurotransmitter in the brain, the patients' symptoms improve. Unfortunately, brain cells become resistant to this substance by passing the time, and treatment stops. Consequently, DBS becomes the second method in Parkinson's disease treatment [3]. DBS is electrode placement in some area of the brain depending on patients' symptoms, and high frequency electrical stimulation by a pulse generator located under the Clavicle bone [5].

M. Sadeghi is with the Islamic Azad University of Iran science and research branch, biomedical engineering faculty (corresponding author to provide phone: 00989125464711; fax:00982144440505; e-mail: mhrzd.sadeghi@ gmail.com).

A.H. Jafari is with the Tehran University Medical Sciences of Iran (e-mail: h_jafari@tums.ac.ir).

In 1980s, DBS was being used in some new parts of Basal Ganglia. Grenoble group for the first time applied high frequency stimulation in ventralis intermedius nucleus of the thalamus for tremor treatment [6]. After a while other disorders like epilepsy, depression, and obsession were treated by this method [7]-[8]-[9].

Stimulation parameters are frequency, pulse width and voltage [10]-[11]. There is not any accurate procedure for the optimizing these parameters and regulating them. Now, this operation is performed by trial and error method, which leads to high cost, patient's inconvenience and time wasting problems. The characteristics of these parameters are degree of freedom, unknown effects and complicated responses [12].

Mechanism of DBS with high frequency is still unknown, but there are some hypotheses to respond. Assuming that Parkinsonian tremor is abnormal oscillation in some regions of the brain, DBS might act to block or interfere with the transmission of oscillatory activity to the motor neurons, or DBS acts to desynchronize these oscillators. Another hypothesis is that DBS might lead to a change in system parameters, and this in turn would lead to a Hopf bifurcation in the dynamics so that the abnormal limit cycle associated with the tremor would be destabilized. This change in system parameters could be related to a gradual change in network properties generating the tremor [13]-[14]-[15].

The aim of this research is to obtain some chaotic features from patients' clinical data whom were under DBS treatment. For every patient chaotic features of tremor in optimal voltages were evaluated and compared with those of other voltages. These features are: embedding space, embedding dimension, correlation dimension, largest Lyapunov exponent, entropy and variance of embedding space along with x, and y axes.

II. Appropriate Selection of Stimulation Parameters

Electrical stimulation parameters comprise frequency, pulse width and voltage that are regulated by a pulse generator placed under the Clavicle bone [5]-[10]-[11]. In order to obtain satisfactory clinical results, optimal parameters hove to

S.M.P. Firoozabadi is with the Tarbiat Modarres University of Iran and the Islamic Azad University of Iran science and research branch (e-mail: purmir@modares.ac.ir).

be selected. These days there is not sufficient information about the function of these parameters on the patients under DBS. In addition to their unknown effects and complicated responses, large degrees of freedom is another problem. The pulse generator of Medtronic's Soletra model 7426 and Itrel II model 7424 use voltages ranging from 0 to 10.5V in 0.115V increments, pulse widths from 60 to 450μs in 30μs increments, and frequencies from 2 to 185HZ (5 to 100HZ in increments of 5HZ and 2,33,130,135,145,160,170, and 185 HZ), so there are 25480 combinations of voltage, frequency, and pulse width [12].

Anatomical targeting and electrical targeting are effective options to select optimal parameters. Anatomical targeting includes determining the location of electrode and determining the location of current flow depending on which neural element (cell or fiber) should be stimulated. Given that stimulation parameters are affected by changing the location of stimulation, selection of stimulation parameters becomes essential [12]-[16].

Electrical targeting affects electrical field distribution and then stimulation parameters in two ways first by electrode geometry, then by electrode location. Every electrode unit consists of four cylindrical electrodes positioned in a row [17]. Electrode geometries include monopolar, bipolar, tripolar, quadripolar, and quintipolar configurations. Depending on each geometry, pulse generator becomes anode and electrodes become anode or cathode. For example in a monopolar geometry, pulse generator is anode and one of the electrodes, depending on the anatomical location of target element, becomes cathode. In a bipolar geometry, two electrodes are determined as anode and cathode. The current flows from anode to cathode, depolarizing the neural elements closest the cathode and hyperpolarizing neural elements nearest the anode. In monopolar geometry which anode and cathode are farther from each other potential distribution occurs in a wide area of tissue. Thus stimulation current has a wider territory and stimulation occurs in a wider territory of the tissue. In bipolar geometry anode and cathode are closer to each other thus potential Distribution is limited to the surrounding area of the cathode, and just small area of the tissue around the cathode is stimulated, which is known as selective stimulation. In tripolar geometry, the stimulation becomes more selective [12]. Equation (1) and equation (2) present potential (φ) in bipolar and monopolar stimulation respectively.

$$\phi = \frac{Id\cos\theta}{4\pi\sigma r^2} \quad (1)$$

Where I is current source, d distance between two electrodes, θ angle between direction of d and the point which potential is obtaining, σ the conductivity, and r distance from the source.

$$\phi = \frac{I}{4\pi\sigma r} \quad (2)$$

Where variable I is current source, σ the conductivity, and r distance from the source.

According to (1) and (2) more voltage gradient descent in bipolar geometry stimulation happens, so it is more selective than monopolar one. Equatio (1) indicates voltage gradient descent is inversely proportional to the square of distance from electrode, but in monopolar stimulation according to (2) this descent gradient is inversely proportional to the electrode distance. Therefore, by increasing the distance, voltage gradient descent in bipolar stimulation is more than monopolar stimulation [18]. Thus, it is more selective, and in order to reach the clinical advantageous, less stimulation is needed in monopolar stimulation, but in bipolar stimulation and tripolar stimulation only the target tissue is stimulated. Because of selective stimulation and more concentrated current neighboring tissues are not stimulated, and it leads to less side effects. This is an advantageous of tripolar and bipolar stimulation [12].

Electrode location is an effective factor on stimulation parameters because space distribution of electrical field depends on electrical properties of electrode's neighboring tissues. The gray matter of central neural system is isotropic (has an equal characteristics in every direction) with conductivity around 0.2 s/m, whereas the white matter is anisotropic composed of fibers with conductivity around 1s/m parallel to the fibers and 0.1s/m perpendicular to the fibers. Therefore, according to which tissue type stimulation electrodes are located in space distribution of electrical field and in turn stimulation parameters change. Now it is clear that stimulation parameters selection depends on many factors. Since there is little knowledge about DBS mechanism and parameter's function, parameters optimization is not easy. These days, selection of these parameters is clinical and is done by trial and error method, so it is cost and time consuming, and leads to patient's inconvenience. Therefore, determining a method for optimum parameter selection, which is done without patient's interference, is valuable and necessary [12].

III. MATERIALS AND METHODS

A. Recording of clinical data

In this research, nine patients' fingers tremor signals who were under DBS were recorded. The signals were recorded without any medicine consumption. Instruments used for this recording included: two piezoelectric accelerometers model 4375, four-channel Amplifier with filtering, A/D card, and a computer.

In order to obtain the tremor signal along with the finger and perpendicular to the finger, two accelerometers were fixed on the two shafts. The shafts were perpendicular to each other. Signals were recorded from that side of body which had started tremor first, also thumb or index fingers were selected depending on which finger had more tremor.

Every patient sat on a chair and his/her hand got fixed on the chair arm in a way that patient's wrist was free. Tremor signal was measured by the accelerometers, amplified and transmitted to an A/D terminal, and saved in a computer by Labview8 software.

Tremor signal was recorded 3 or 4 times for every patient. Frequency and pulse width in every patient's recordings was constant and determined by neurologist whereas voltage was variable. One of the voltages was optimal voltage determined by neurologist comment.

B. Data filtering

After obtaining data it was filtered in several stages, such as;

1) By using a lowpass filter designed in the amplifier frequencies higher than 15Hz were filtered while recording.

2) A forth order Butterworth filter was designed and used while saving data by Labview8 software, frequencies over 10Hz were filtered.

3) Since the frequency of parkinsonian patient tremor is 4 to 6Hz, an Elliptic bandpass filter designed by Matlab2007 software was used to filter frequencies lower than 0.5Hz and upper than 8Hz.

C. Chaos features

In order to get optimal stimulation parameters in a nonclinical way, some famous chaotic features were used in this research. The features were: embedding space, embedding dimension, correlation dimension, largest Lyapunov exponent, entropy and variance of embedding space along with x, y axes. By Matlab2007 software and Tstools toolbox these features were calculated for recorded tremor signals.

IV. RESULTS

For one of the patients, embedding spaces at different voltages are shown in Fig. 1 and chaos calculated features of that patient data are represented in table I. Fig. 1(a), (b), (c) are embedding spaces related to frequency of 135Hz, pulse width of 60μs for all of them and voltages of 1V, 1.4V, 1.7V respectively. For this patient voltage of 1.7V is the optimum voltage according to the neurologist comment. As in Fig. 1(a), (b), (c) tremor embedding space has an attractor and in Fig.1 (c) which is related to embedding space of tremor in optimal voltage, this attractor is the strongest. This strong attractor can help us to recognize optimal voltage from the others.

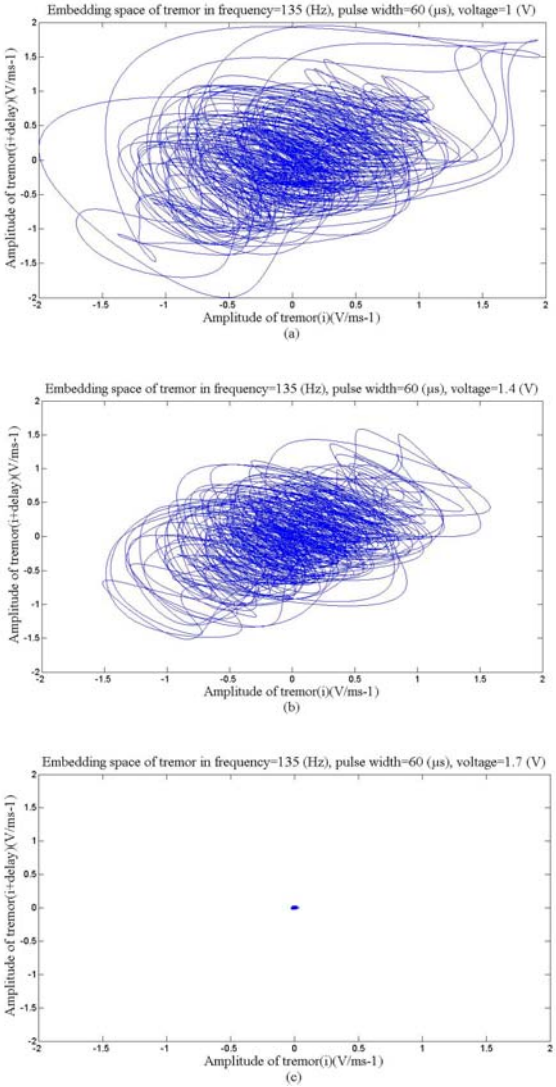

Fig. 1 Embedding spaces of tremor data related to Voltages=1(V), 1.4(V), 1.7 (V).

TABLE I
CHAOTIC FEATURES OF TREMOR DATA AT VOLTAGES=1(V), 1.4(V), 1.7(V)

Voltage	Correlation dimension	Fractal dimension	Entropy	Largest Lyapunov exponent	Variance of embedding space along with x axes	Variance of embedding space along with y axes
1	1.8947	1.6105	2.9660	0.0881	0.3242	0.3243
1.4	1.9478	1.567	2.3647	0.0924	0.2339	0.2340
1.7	1.8833	1.129	0.5490	0.0508	6.0762e-005	6.0812e-005

Regarding the table I the largest Lyapunov exponent is positive, which shows the chaotic behavior of tremor signal under DBS. Also, entropy value of tremor signal is minimum in optimal voltage. Therefore, this minimum value can be applied as another technique to find optimal voltage. The values of tremor signal embedding space variances along with x, and y axes are minimums in optimal voltage. Since amplitude of tremor is minimum in optimal voltage because of more treatment, so minimum values of variance of embedding space is expected. This value also can be another solution to recognize optimal voltage.

V. CONCLUSION

Parkinson's disease is the most common movement disorder that is mostly seen in old people. DBS is the second method for treatment of this disease, which is applied after medical treatment and includes electrodes placement in the brain and electrical stimulation. Electrical stimulation comprises three parameters: frequency, pulse width and voltage. In order to achieve the best treatment the stimulation parameters should be selected properly. This is performed clinically currently by trial and error method by neurologists.

In this research, the tremor signal was processed after recording. Chaotic features of the signals were compared with each other at different voltages. The features were embedding space, embedding dimension, correlation dimension, largest Lyapunov exponent, entropy and variance of embedding space along with x, and y axes.

Some of the chaotic features like entropy and variance of embedding space differ remarkably in optimal voltages, which leads to recognize the optimal voltage for stimulation without patient interference. This method is current paper's main advantageous.

Since the main cause of this disease and DBS mechanism is still unknown, it is expected to obtain numerical methods for optimizing stimulation parameters. In order to clinically overcome the problems of clinically parameter estimation (time and cost consuming and patient's inconvenience), more physiological information shall be gathered.

REFERENCES

[1] H. Yu, J. S. Neimat, "The Treatment of Movement Disorders by Deep Brain Stimulation", Vol. 5, 26–36, January 2008 © The American Society for Experimental NeuroTherapeutics, Inc.

[2] S. S. HACISALIHZADE, M. MANSOUR, C. Albani, "Optimization of Symptomatic Therapy in Parkinson's Disease", IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, VOL. 36, NO. 3, MARCH 1989.

[3] M. Haeri, Y. Sarbaz, Sh. Gharibzadeh, "Modeling the Parkinson's tremor and its treatments", Journal of Theoretical Biology 236, 311–322, 2005.

[4] A. H. V. Schapira, E. Bezard, J. Brotchie, F. Calon, G. L. Collingridge, B. Ferger, et al.," Novel Pharmacological Targets for the Treatment of Parkinson's Disease" NATURE REVIEWS DRUG DISCOVER, OCTOBER 2008.

[5] C. R. Butson, C. C. McIntyre, "Differences among implanted pulse generator waveforms cause variations in the neural response to deep brain stimulation", Clinical Neurophysiology 118 (2007) 1889–1894.

[6] S. Breit, J.B. Schulz , A.-L. Benabid, "Deep brain stimulation", Cell Tissue Res (2004) 318: 275–288, DOI 10.1007/s00441-004-0936-0.

[7] Th. Wichmann, M.R. DeLong, "Deep Brain Stimulation for Neurologic and Neuropsychiatric Disorders", Neuron 52, 197–204, October 5, 2006 ª2006 Elsevier Inc. DOI 10.1016/j.neuron.2006.09.022.

[8] D. S. Kern, R. Kumar, "Deep Brain Stimulation", The Neurologist • Volume 13, Number 5, September 2007.

[9] T. Fiegele, G. Feuchtner, F. Sohm, R. Bauer, J. V. Anton, T. Gotwald and et al "Accuracy of stereotactic electrode placement in deep brain stimulation by intraoperative computed tomography"., Department of Neurosurgery, Innsbruck Medical University, Anichstrasse 35, 6020 Innsbruck, Austria b Department of Radiology II, Innsbruck Medical University, Innsbruck, Austria Received 16 August 2007; received in revised form 13 November 2007; accepted 3 January 2008

[10] L. Garcia1, G. D'Alessandro2, B. Bioulac1 and C. Hammond2 "High-frequency stimulation in Parkinson's disease: more or less? " Laboratoire de neurophysiologie (Centre National de la Recherche Scientifique UMR 5543), Universite´ de Bordeaux 2, 146 rue Le´o Saignat, 33076 Bordeaux Cedex, France 2Institut de Neurobiologie de la Me´ diterrane´e (Institut National de la Recherche Me´ dicale U 29), 163 route de Luminy, BP 13, 13273 Marseille Cedex 9, France

[11] J. E. Arle and J. L. Shils "Motor Cortex Stimulation for Pain and Movement Disorders" Department of Neurosurgery, Lahey Clinic, Burlington, Massachusetts 01805, and Department of Neurosurgery, Tufts University School of Medicine, Boston, Massachusetts 02110

[12] A. M. Kuncel, W. M. Grill, "Selection of stimulus parameters for deep brain stimulation", Clinical Neurophysiology 115 (2004) 2431–2441.

[13] Erwin B. Montgomery Jra,_, John T. Galeb "Mechanisms of action of deep brain stimulation (DBS)" Department of Neurology, National Primate Research Center, University of Wisconsin–Madison, H6/538 CSC, 600 Highland Ave., Madison, WI 53792, USA Department of Neurosurgery, Massachusetts General Hospital/Harvard Medical School, Edwards Research Building, EDR 410, 50 Blossom St., Boston, MA 02114, USA

[14] J. Y. Chang, L. H. Shi, F. Luo, W.M. Zhang, D.J Woodward, "Studies of the neural mechanisms of deep brain stimulation in rodent models of Parkinson's disease" , Neuroscience and Biobehavioral Reviews 31 (2007) 643–657.

[15] M.S. Titcombe, L. Glass, A. Beuter , "Dynamics of Parkinsonian tremor during deep brain stimulation", American Institute of Physics, DECEMBER 2001.

[16] T. O. Videen, M. C. Campbell , S. D. Tabbal, M. Karimi, T. Hershey, J. S. Perlmutter, "Validation of a fiducial-based atlas localization method for deep brain stimulation contacts in the area of the subthalamic nucleus", Department of Neurology, Washington University School of Medicine, St. Louis, MO 63110, USA Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, MO 63110, USA Department of Psychiatry, Washington University School of Medicine, St. Louis, MO 63110, USA Department of Anatomy & Neurobiology, Washington University School of Medicine, St. Louis, MO 63110, USA Program in Physical Therapy, Washington University School of Medicine, St. Louis, MO 63110, USA Received 7 June 2007; received in revised form 11 October 2007; accepted 11 October 2007

[17] B. Blad, L. Bertenstam, S. Rehncrona, H. Bjartmarz, A.-L. Törnqvist, "Measurement of contact impedance of electrodes used for deep brain stimulation", ITBM-RBM 26 (2005) 344–346.

[18] D. M. Durand, "Electrical Stimulation of Excitable Systems" case western reserved university