Dynamic Tension EMG to Characterize the Effects of DBS Treatment of Advanced Parkinson's Disease

V. Ruonala*, E. Pekkonen, S. Rissanen, O. Airaksinen, G. Miroshnichenko, M. Kankaanpää, P. Karjalainen

Abstract— **Deep brain stimulation (DBS) is an effective treatment method for motor symptoms of advanced Parkinson's disease. DBS-electrode is implanted to subthalamic nucleus to give precisely allocated electrical stimuli to brain. The optimal stimulus type has to be adjusted individually. Disease severity, main symptoms and biological factors play a role in correctly setting up the device. Currently there are no objective methods to assess the efficacy of DBS, hence the adjustment is based solely on clinical assessment. In optimal case an objectively measurable feature would point the right settings of DBS. Surface electromyographic and kinematic measurements have been used in Parkinson's disease research. As Parkinson's disease symptoms are known to change the EMG signal properties, these methods could be helpful aid in the clinical adjustment of DBS. In this study, 13 patients with advanced Parkinson's disease who received DBS treatment were measured. The patients were measured with seven different settings of the DBS in clinical range including changes in stimulation amplitude, frequency and pulse width. The EMG analysis was based on parameters that characterize EMG signal morphology. Correlation dimension and recurrence rate made the most significant difference in relation to optimal settings. In conclusion, EMG analysis is able to detect differences between the DBS setups, and can help in finding the correct parameters.**

I. INTRODUCTION

Parkinson's disease is a progressive neuromotoric disease mainly among the old, and it has an estimated prevalence of 1% in those over 60 years of age in industrialized countries [1]. The main symptoms of the disease are resting tremor, bradykinesia, rigidity and postural instability along with other non-motor symptoms. Currently there is no cure, nor treatment to stop the progression of Parkinson's disease. Nonetheless, with appropriate medication the life quality and active life time of the patients lengthens significantly. Dopamine antagonist medication is the most widely used treatment for the Parkinson's disease. While medication is known to have better therapeutic response to rigidity and bradykinesia than to tremor, it loses it effectiveness during time.

This work was supported by Academy of Finland under project 252748.

*V. Ruonala, S. Rissanen, G. Miroshnichenko and P. Karjalainen are with the Department of Applied Physics, University of Eastern Finland, FI-70211 Kuopio, Finland (email: verneri.ruonala@uef.fi)

E. Pekkonen is with the Department of Neurology and with the BioMag Laboratory, Helsinki University Central Hospital, FI-00029 Helsinki, Finland

O. Airaksinen is with the Department of Physiology and Rehabiliation Medicine, Kuopio University Hospital, FI-70211 Kuopio, Finland

G. Miroshnichenko is with the Petrozavodsk State University of Petrozavodsk, Russian Federation

M. Kankaanpää is with the Department of Physiology and Rehabiliation Medicine, Tampere University Hospital, FI-33521 Tampere, Finland

When the medication response retracts, chronic deep brain stimulation (DBS) of subthalamic nucleus (STN) can be effective way to treat the motor symptoms of Parkinson's disease. It eases all the cardinal motor symptoms in patients with advanced Parkinson's disease: tremor, rigidity and bradykinesia [2], and also allows for reduction in anti-parkinsonian medication doses [3]. In DBS an electrode is positioned into subthalamic nucleus where it gives constant pulsed stimulation to surrounding brain regions.

The mechanism of action of DBS is currently unclear, one theory suggested by *Montgomery et al.* is that DBS affects to oscillatory loops in motor control system of the brain. In successful treatment, DBS provokes excitation of some neural elements while preventing the excitation of others. The main parameters that affect DBS efficacy are the location of stimulation electrodes, pulse details and individual differences in brain anatomy. [4]

During the adjustment session of DBS the adjustment is done by altering pulse properties: voltage amplitude, frequency and width. The correct combination of these parameters has to be set to allow the stimulator work efficiently. The adjustment of the DBS-stimulator is currently done by clinician observation. The optimal stimulator settings may be problematic to find because there is vast amount of different possible combinations of parameters and some combinations can induce adverse effects.

Surface electromyographic (EMG) and kinematic methods are appealing since they are noninvasive, easy to produce and cost effective. These methods have been used in differentiating patients with Parkinson's disease from healthy controls [5], differential diagnosis of PD and other diseases [6], [7] and quantification of treatment methods [8], [9]. The EMG signal of patients with Parkinson's disease has been found to contain more rhythmic bursts and tonic activity than healthy controls [5]. EMG analysis could be a suitable method for detecting the changes in motor control while adjusting the DBS.

There are some studies that focus on EMG in DBS patients [9], [10], but they lack information about the adjustment of DBS to get optimal response. In addition there are some kinematic studies about adjusting DBS, *O'Suilleabhain et al.* studied kinematic response to the change of DBS stimulation voltage in 1 V steps from 0 to 4 V and found that tremor responded asymptotically to increasing stimulus voltage [11].

In this work EMG signals of 13 patients with Parkinson's disease who were treated with DBS were measured during dynamic contraction of elbow joint. The measurements were done with 7 different settings of DBS altering the pulse am-

978-1-4244-7929-0/14/$26.00 ©2014 IEEE

plitude, frequency and pulse width in clinical range. To our knowledge, this is one of the first studies to assess the EMG of DBS in clinical range. The aim of this work is to determine if EMG can detect the alteration of DBS parameters in a clinical range during DBS adjustment. Secondary aim is to determine if these alterations can be used to assist a clinical doctor while adjusting the DBS.

II. Methods

A. Subjects

EMG measurements were done to 13 (2 female) patients with Parkinson's disease. The patients had a diagnosis of idiopathic Parkinson's and previously implanted DBS (Kinetra or Activa PC Neurostimulators, Medtronic Inc, Minneapolis, USA). The patients gave an informed consent before the measurements. The study was approved by the local human ethics committee of the Kuopio University Hospital. The measurements were done by a same person at the same place (BioMag laboratory, Helsinki). The age of the patients was (58±11) years and they had had the disease for (11±5) years. The severity of the disease measured in total Unified Parkinson's Disease Rating scale (UPDRS) motor score (ranging 0-108) points was (36±12) for the patients when the stimulator was off and (23±8) when the stimulator was on.

B. Measurements protocol

The measurement began with UPDRS motor score assessment with the DBS in formerly adjusted optimal settings. EMG was used to observe the effects of DBS with different settings. Before attaching the electrodes, the skin beneath them was properly cleaned with ethanol wetted cotton pads. Disposable Ag/AgCl surface electrodes (Medicotest M-00-S) were placed to the belly and 3 cm below the belly of the biceps brachii muscle of both hands. The reference electrode was placed to an inactive point on the lateral side of brachium, approximately 6-7 cm from the recording electrodes. Triaxial accelerometer (MEAC-X, ± 10 g Mega Electronics) was attached to anterior side of the forearm, halfway between the wrist and the elbow to record the movement of hands during the measurement. The signals were recorded with ME6000 biosignal monitor (Mega Electronics Ltd., Kuopio, Finland) with sampling rate 1000 Hz. The resolution was 1 µV for EMG acquisition and 2 mg for acceleration acquisition.

The patients had their current normal medication throughout the measurement. During the measurements the patients were sitting on an ordinary chair without armrests. The task was to do biceps flexion and extension with elbow staying at place. The task consisted of 7–8 repetitions and was completed separately on each hand. The patients were instructed about the course of the measurement beforehand, and they were let practice shortly the task to get used to the measurement setup.

The first measurement was done with the DBS at optimal settings. Optimal settings refer to the DBS settings which the patient had on their stimulator before the study. Then the settings were changed and the task repeated. After changing the stimulator settings, the status of the patient was let to stabilize minimum of three minutes as some effects of the stimulator might be unstable for first few minutes. Before each measurement, the tremor and rigidity of hands and feet was evaluated. The protocol was repeated with different setups relative to the optimal settings with randomized order: amplitude -0.3 V and $+0.3$ V, frequency -30 Hz and $+30$ Hz, and pulse width $+30$ µs. In the last phase the task was repeated with DBS off. After DBS off measurement the UPDRS assessment was done second time.

If there were adverse effects which were too hard to bear within the measurement, the measurement in that DBS setup was aborted and the optimal settings returned. This happened several especially when DBS pulse width was increased and when it was turned off.

C. Analysis

In the preprocessing phase the EMG signals were lowpass filtered with 9th order butterworth filter with cutoff 150 Hz to remove non EMG based noise. Then smoothness priors detrending method [12] was used to remove low frequency variation from the signals. Last preprocessing step was to remove the powerline and DBS induced noise. It was done by spectrum interpolation ±2 Hz around 50 Hz and around DBS stimulator frequency.

The difference in EMG and signals between different settings were sought from various parameters characterizing the morphology of EMG. Correlation dimension (D2) is a measure which describes the complexity of the signal. Recurrence rate (%REC) is the amount of recurring structures in the signal. Wavelet maximum (W_m) is calculated as the maximum of wavelet transform coefficients and is related to the amount of recurrent waveforms in the signal. D2 and %REC are known to differ in Parkinson's disease patients in relation to healthy controls [13].

The EMG and signals were divided to segments that consist only the flexion part of the dynamic task. The parameters were calculated separately for each flexion and then averaged to get the value. The calculation of D2, %REC and Wmax is explained in more detail in [13], [5]. The differences between the settings were compared individually against the optimal settings of the stimulator. The results were concluded with group based analysis between the different setups. Wilcoxon signed rank sum test was used to determine significances of the results.

III. Results

There was no substantial change in hand tremor or rigidity in patients within the measurement. Some patients did not react to DBS adjustment even when the stimulator was turned off. Generally the tremor and rigidity were stronger on the right hand side and the rigidity was more commonly observed than tremor with the optimal setup. The most significant increase relative to optimal setup was observed when the stimulator was turned off. Even though the deviation in the scores is considerable, some patterns can be

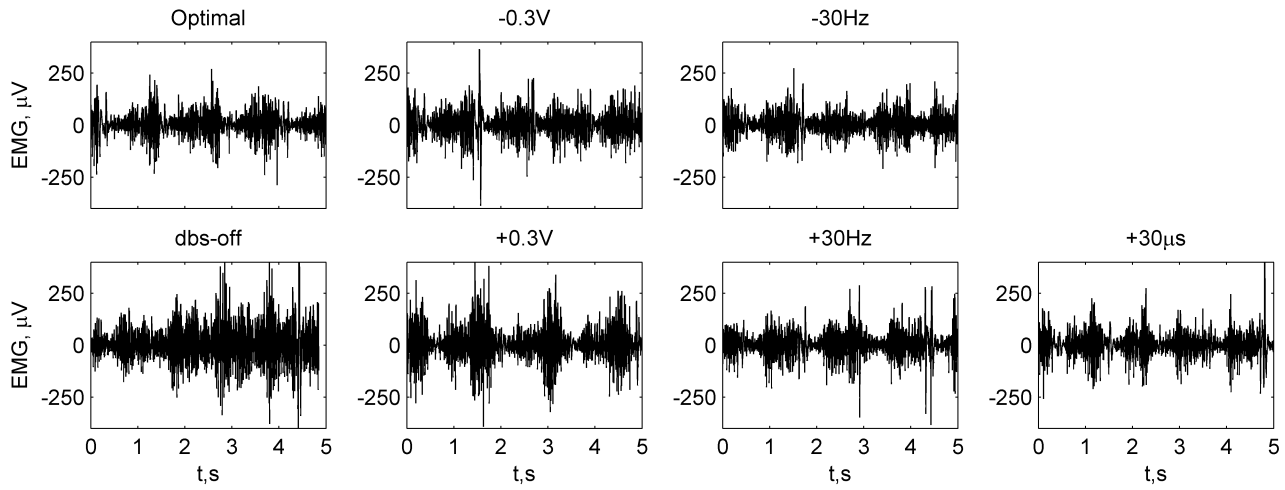

Fig. 1. EMG signal during dynamic tension of arm with different DBS setups.

observed: on right hand side the tremor and rigidity increase when decreasing amplitude or frequency, and decrease when increasing amplitude or frequency. Similar behavior is observed in left hand tremor and rigidity, but it is not as clear.

The measurements were checked visually before the parameter analysis. The EMG signals of one patient in different DBS settings are presented in Fig. 1. Overall the measurement showed wide variety of responses to DBS adjustment from greater differences to no difference. When comparing the responses, the greatest difference between the settings was observed between the DBS-off setup. In Fig. 1 it is noted that the DBS modifies the shape and the amplitude of the bursts.

Calculated parameters D2, %REC and Wmax are shown in Tbl. I. There is considerable amount of variation between patients in the calculated parameters. D2 shows the most significant difference between the optimal case and other setups, only A_{-} does not significantly differ from the optimal case. The other parameters show significant difference in part of setups only. D2 and Wmax values peak at optimal settings, changing any parameter will lower the values. %REC increases when changing the settings from optimal case.

IV. Discussion

In this novel study patients with DBS were assessed in different stimulator setups with EMG. It was observed that there are EMG characteristics which differ between the setups. However, the response varied large amount between the subjects.

The subjects had a diagnosis of idiopathic Parkinson's disease and they had been treated with DBS at least for three months before the measurement. This is usually considered to be long enough time for the physical lesions to heal after the surgery. The disease progression of the patients was different as was their current condition. Some patients had severe symptoms of Parkinson's disease while others were in quite good condition when bearing in mind that they receive DBS treatment. The patients had different reasons for installing DBS: on-off phases, rigidity and hand tremor. This explains the differences in tremor and rigidity responses, for some patients there was no change in rigidity nor tremor throughout the measurement while others reacted clearly to changing setup of DBS.

The visual analysis of the EMG signals during dynamic tension showed wide variety of responses to different settings of DBS. In some patients there was virtually no change in EMG while adjusting the DBS whereas in some patients the changes were extensive. This is seen also in the UPDRS motor points, there were four patients with only slight or none change in hand rigidity and tremor. For some patients the DBS eases the off-phases of medication response and the symptoms may not be present unless they are experiencing this off-phase.

The dynamic EMG signals were quantified with parameter analysis to detect differences between the setups of DBS. Several different linear and nonlinear parameters were evaluated, but very few of them managed to detect the difference between the setups. Previously nonlinear parameters have been used to differentiate Parkinson's disease from healthy controls. It is likely that the differences between the DBS setups are observed in nonlinear parameters. Signal correlation dimension provided the most significant difference between the different setups, while recurrence rate and wavelet maximum coefficient did differ significantly in only some cases. According to results, the decrease of $0.3\,\mathrm{V}$ in amplitude is hardest to detect and none of the parameters calculated could sense a significant difference in group based analysis.

The results are convincing, all the parameters have their minimum or maximum value when DBS setup is at optimal settings. The values do not follow the UPDRS scores strictly, as the lowest UPDRS points were observed when amplitude or frequency was increased. However, the situation has more sides to it, usually increasing the amplitude or frequency brought other adverse effects to the patient and it was not

TABLE I

TREMOR AND RIGIDITY SCORES OF LEFT (LH) AND RIGHT (RH) HAND AND PARAMETERS WITH DIFFERENT SETUPS OF DBS (IN PARAMETERS, WILCOXON TEST USED TO DETERMINE SIGNIFICANT DIFFERENCES VERSUS OPTIMAL SETUP A_0 *=P<0.05, ** =P<0.01).

DBS setting	A_0	A_-	A_+	F_-	F_+	W_+	OFF
UPDRS							
LH tremor	0.1 ± 0.3	0.3 ± 0.7	0.0 ± 0.0	0.3 ± 0.7	0.1 ± 0.3	0.1 ± 0.4	0.6 ± 0.7
RH tremor	0.3 ± 0.7	0.8 ± 1.2	0.1 ± 0.3	0.8 ± 1.1	0.1 ± 0.3	0.3 ± 0.8	1.1 ± 1.6
LH rigidity	0.5 ± 0.7	0.6 ± 0.8	0.2 ± 0.6	0.4 ± 0.5	0.2 ± 0.4	0.1 ± 0.4	0.8 ± 1.0
RH rigidity	0.6 ± 1.0	0.8 ± 1.3	0.2 ± 0.4	0.7 ± 1.1	0.6 ± 1.0	0.22 ± 0.5	1.4 ± 1.3
Param.							
D2	3.57 ± 0.58	3.48 ± 0.47	3.31 ± 0.70*	3.27 ± 0.57**	3.41 ± 0.52*	3.28 ± 0.41*	3.32 ± 0.66*
REC	6.93 ± 5.07	7.20 ± 3.91	9.18 ± 7.16	8.62 ± 5.23**	7.73 ± 4.09	7.93 ± 2.94*	9.85 ± 6.61*
Wmax	8.04 ± 0.95	7.99 ± 1.01	7.76 ± 0.97*	7.82 ± 0.90	7.95 ± 0.88	7.36 ± 1.07*	7.80 ± 1.11

possible use that setup permanently. While the group based analysis shows good results, the variation in the values is considerable. The group based analysis will point out the general behavior of parameters, but might not apply for every patient individually, which is the ultimate aim for the EMG DBS studies.

The DBS setups for the study were chosen so that they represent typical DBS adjustment session, only slight changes to one parameter at time. Steps smaller than $\pm 0.5\,\mathrm{V}$ are normally used when seeking the correct setup for DBS. The changes are very small and the effect on signals may be subtle, but appropriate for the symptoms. It is assumed that if the amplitude and frequency were changed in larger steps, also the effects would be more visible in EMG signal. However the scope of this study was to determine if EMG can detect changes in clinical range.

The measurements were done on medication to assure patient safety during the measurement. This might weaken the results as the medication decreases the symptoms, but it has been observed that while the medication is able to reduce the Parkinson's disease indications in EMG signal, it has not been able to discard them [14], [15].

The main aim of the study was to determine if EMG can detect changes when DBS stimulator settings are changed. There are clear changes in the EMG signals of the patients. However there are individual differences how the DBS affects to the signals. The secondary aim was to determine if the differences can be used to assist the clinical adjustment of the DBS device. The results indicate that the parameters follow U-shaped response suggested by *Montgomery et al* [4] and the optimal amplitude and frequency is found at the bottom (or top) of the curve. In conclusion, this novel study shows that EMG analysis of dynamic task can be useful when determining the suitable DBS parameters for some patients.

REFERENCES

[1] L. de Lau and M. Breteler, "Epidemiology of Parkinson's disease," *Lancet Neurol.*, vol. 5(6), pp. 525–535, 2006.

[2] Deep Brain Stimulation for Parkinson's Disease Study Group, "Deep-brain stimulation of the subthalamic nucleus or the pars interna of the globus pallidus in Parkinson's disease," *New Engl. J. Med.*, vol. 345, no. 13, p. 956, 2001.

[3] A. Benabid, S. Chabardes, J. Mitrofanis, and P. Pollak, "Deep brain stimulation of the subthalamic nucleus for the treatment of Parkinson's disease," *Lancet Neurol.*, vol. 8(1), pp. 67–81, 2009.

[4] E. B. Montgomery Jr and J. T. Gale, "Mechanisms of action of deep brain stimulation (DBS)," *Neurosci. Biobehav. R.*, vol. 32, no. 3, pp. 388–407, 2008.

[5] S. Rissanen, M. Kankaanpää, M. Tarvainen, A. Meigal, J. Nuutinen, I. Tarkka, O. Airaksinen, and P. Karjalainen, "Analysis of dynamic voluntary muscle contractions in Parkinson's disease," *IEEE Trans. Biomed. Eng.*, vol. 56(9, pp. 2280–2288, 2009.

[6] B. Hellwig, P. Mund, B. Schelter, B. Guschlbauer, J. Timmer, and C. Lücking, "A longitudinal study of tremor frequencies in Parkinson's disease and essential tremor," *Clin. Neurophysiol.*, vol. 120, no. 2, pp. 431–435, 2009.

[7] M. Muthuraman, A. Hossen, U. Heute, G. Deuschl, and J. Raethjen, "A new diagnostic test to distinguish tremulous Parkinson's disease from advanced essential tremor," *Mov. Disord*, vol. 26, no. 8, pp. 1548–1552, 2011.

[8] M. Sturman, D. Vaillancourt, L. Metman, R. Bakay, and D. Corcos, "Effects of subthalamic nucleus stimulation and medication on resting and postural tremor in Parkinson's disease," *Brain*, vol. 127(9), pp. 2131–2143, 2004.

[9] S. Rissanen, M. Kankaanpää, M. Tarvainen, V. Novak, P. Novak, K. Hu, B. Manor, O. Airaksinen, and P. A. Karjalainen, "Analysis of EMG and acceleration signals for quantifying the effects of deep brain stimulation in Parkinson's disease," *IEEE T. Bio-med. Eng*, vol. 58, no. 9, pp. 2545–2553, 2011.

[10] J. Levin, S. Krafczyk, P. Valkovič, T. Eggert, J. Claassen, and K. Bötzel, "Objective measurement of muscle rigidity in parkinsonian patients treated with subthalamic stimulation," *Mov. Disord.*, vol. 24(1), pp. 57–63, 2009.

[11] P. E. O'Suilleabhain, W. Frawley, C. Giller, and R. B. Dewey, "Tremor response to polarity, voltage, pulsewidth and frequency of thalamic stimulation," *Neurology*, vol. 60, no. 5, pp. 786–790, 2003.

[12] M. Tarvainen, P. Ranta-aho, and P. Karjalainen, "An advanced detrending method with application to HRV analysis," *IEEE Trans. Biomed. Eng.*, vol. 49(2), pp. 172–175, 2002.

[13] S. Rissanen, M. Kankaanpää, A. Meigal, M. Tarvainen, J. Nuutinen, I. Tarkka, O. Airaksinen, and P. Karjalainen, "Surface EMG and acceleration signals in Parkinson's disease: feature extraction and cluster analysis," *Med. Biol. Eng. Comput.*, vol. 46, pp. 849–858, 2008.

[14] C. Blahak, J. Wöhrle, H.-H. Capelle, H. Bäzner, E. Grips, R. Weigel, M. Hennerici, and J. Krauss, "Tremor reduction by subthalamic nucleus stimulation and medication in advanced Parkinson's disease," *J. Neurol.*, vol. 254(2), pp. 169–178, 2007.

[15] J. Robichaud, K. Pfann, C. Comella, and D. Corcos, "Effect of medication on EMG patterns in individuals with Parkinson's disease," *Mov. Disord.*, vol. 17(5), pp. 950–960, 2002.