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### $A\ R\ T\ I\ C\ L\ E\ \ I\ N\ F\ O$

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## ABSTRACT

Aim of the study: We present the preliminary results of the study focused on the impact of subthalamic deep brain stimulation (DBS-STN) on sleep and other non-motor symptoms (NMS).

Materials and methods: Ten patients with advanced PD, underwent two-night polysomnography (PSG) mean 1.1 week before surgery and 6.2 months post DBS programming. NMS were assessed with a set of scales before surgery and 6 months and 12 months following DBS programming.

Results: Contrary to previous studies, we noted deterioration of sleep pattern in the followup PSG. We found a decrease in total sleep time, duration of the stage N2, with prolongation of stage N1 and wakefulness after sleep onset. We did not detect any impact of DBS-STN on subjective severity of restless legs syndrome. REM – sleep behavior disorder, however reported was not observed in any patient during PSG evaluations. We also found statistically significant correlations between severity of sleep disturbances and quality of life, as well as, between severity of motor symptoms and worse objective sleep quality.

*Conclusions*: We found that DBS-STN improved quality of life, subjective quality of sleep and sleepiness, however, contrary to the previous studies the objective parameters of sleep worsened after the surgery.

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## <sup>20</sup> **1. Introduction**

21 Parkinson's disease (PD) is a progressive neurodegenerative disorder traditionally viewed as a primarily motor entity, 22 23 however, the spectrum of non-motor symptoms (NMS) is wide and includes neuropsychiatric disturbances, cognitive deteri-24 25 oration, sensory symptoms, autonomic dysfunction and sleep 26 and wakefulness disorders [2,3]. Many studies demonstrated 27 that NMS determine quality of life (QoL) and are more debilitating than motor symptoms [3,4]. Among NMS sleep 28 29 disturbances are one of the most important contributors to poor quality of life of patients and their caregivers [5,6]. 30

Initial studies on the efficacy of deep brain stimulation
(DBS) in PD focused almost solely on motor aspects and the
influence of STN (subthalamic nucleus) targeted DBS on NMS
and particularly sleep is the matter of only a few recent studies
including a small groups of patients.

Hence, we aim to explore effects of DBS-STN in PD patients,with special emphasis on sleep.

## <sup>38</sup> 2. Material and methods

39 Ten advanced PD patients, 6 females and 4 males, with the mean age of 59  $\pm$  8 years (range 45–68) and the mean disease 40 duration of  $11 \pm 2$  years, who fulfilled the Defer et al. [7] CAPSIT 41 42 - criteria to perform a routine DBS therapy (no preselection), were included into the study. During preoperative evaluation 43 44 patients were hospitalized and underwent comprehensive neuropsychological assessment (including Beck Depression 45 Inventory, BDI), brain magnetic resonance imaging and 46 47 levodopa challenge test. Non motor symptoms were assessed with the use of Non-Motor Symptoms Scale (NMSS), Parkin-48 son's Disease Sleep Scale (PDSS), Epworth Sleepiness Scale 49 50 (ESS), Single-Question Screen for RBD (RBD1Q), Parkinson's 51 Disease Quality of Life Questionnaire (PDQ-39). Patients who 52 fulfilled criteria of International RLS Study Group for the 53 diagnosis of RLS were additionally examined with Interna-54 tional RLS Study Group Rating Scale (IRLS). Patients were 55 evaluated on two consecutive nights with PSG at a median of 1.1 week before surgery and again at a median of 6.2 months 56 post DBS programming. The first nights were considered to be 57 adaptation nights and the obtained data were not analyzed, 58 except for 2 patients whose recordings from the second nights 59 60 were not valid due to the technical issues. All PSG studies were 61 conducted in the sleep laboratory in the psychiatry clinic by a 62 PSG technician and scored by a physician certified in sleep medicine (Polish Sleep Research Society Certificate). During 63 the PSG recordings we used 2 EOG channels, 6 EEG channels 64 (F3-A2, F4-A1, C3A2, C4-A1, O1-A2, O2-A), 3 EMG channels, 2 65 limb movement channels, 1 airflow channel, 1 ECG channel 66 and 1 oximetry channel. DBS programming was performed at a 67 68 median of 7 weeks post DBS implantation. The follow-up 69 outpatient evaluations were performed 6 months and 12 months following DBS programming. We used the Shapiro-70 71 Wilk test to check whether the data followed normal 72 distribution, then parametric (t-test) and non-parametric (Wilcoxon signed-rank and Mann-Whitney-Wilcoxon) tests 73 74 accordingly. We searched for correlations with the use of Kendall and Spearman's rank correlation coefficient (Kendall's tau coefficient and Spearman's rho). The study was approved by Independent Bioethics Commission for Research and we obtained written informed consent from all patients.

### 3. Results

DBS-STN in a statistically significant manner (p < 0.05) reduced total sleep time and duration of the stage N2, lengthened duration of the stage N1 and of the wake after sleep onset (WASO). Moreover, an increase of the arousal index (AI), improvement of the periodic limb movements index (PLMI) and the apnea hypopnea index (AHI) were observed, though these changes were not statistically significant. No findings typical of RBD were found on PSG evaluations and REM atonia was preserved in all ten subjects.

The details of the subjects' characteristics compiled with PSG data are presented in Table 1 and the complete results of Q2 the preoperative and follow-up polysomnographic recordings along with other non-motor and motor scales are displayed in Table 2.

DBS-STN in a statistically relevant way alleviated nonmotor symptoms scores (NMSS) and improved quality of life (PDQ39). DBS-STN improved subjective measures of sleep quality (PDSS) and reduced sleepiness (ESS), however, these differences were not statistically significant. Four out of ten patients fulfilled the criteria of International RLS Study Group for the diagnosis of RLS throughout the study and their symptoms remained relatively stable at follow up. At the initial evaluation and 6 and 12 months follow-ups, six, five and eight patients, respectively, were suspected of RBD based on interview and a positive answer to RBD1Q.

We found statistically significant negative relationships between severity of subjective sleep disturbances (PDSS), NMSS scores and quality of life (PDQ39). We also demonstrated significant negative correlations between the severity of motor symptoms (UPDRS part III) and objective sleep quality (as assessed by sleep efficiency and WASO).

We did not detect any correlations between RLS (IRLS) and sleep efficiency, sleep efficiency or RLS, age, disease duration or dominant side and severity of non-motor symptoms.

## 4. Discussion

Until now there have been only six studies published with the polysomnography (PSG) evaluation in PD patients treated with DBS-STN [7–12]. These studies were based on different designs and most of them included small number of patients (from 5 up to 11) and only the recent one included 50 patients [11], therefore making it difficult to compare their results. Generally, DBS-STN was found to increase the duration of total sleep time and deep sleep, improve sleep efficiency, decrease WASO, whereas in most cases PLMS, RBD and RLS remained unchanged. Table 3 presents the most important findings in the previous 6 studies.

In our patients we found an improvement in subjective measures of sleep, as assessed by PDSS and NMSS subdivision for sleep, as well as reduced sleepiness on the ESS. However, 100

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