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Short communication

The impact of subthalamic deep brain stimulation on polysomnographic sleep pattern in patients with Parkinson's disease – Preliminary report

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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 follow-up 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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1. Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder traditionally viewed as a primarily motor entity, however, the spectrum of non-motor symptoms (NMS) is wide and includes neuropsychiatric disturbances, cognitive deterioration, sensory symptoms, autonomic dysfunction and sleep and wakefulness disorders [1,2]. Many studies demonstrated that NMS determine quality of life (QoL) and are more debilitating than motor symptoms [2,3]. Among NMS sleep disturbances are one of the most important contributors to poor quality of life of patients and their caregivers [4,5].

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.

2. Material and methods

Ten advanced PD patients, 6 females and 4 males, with the mean age of 59 ± 8 years (range 45–68) and the mean disease duration of 11 ± 2 years, who fulfilled the Defer et al. [6] CAPSIT – criteria to perform a routine DBS therapy (no preselection), were included into the study. During preoperative evaluation patients were hospitalized and underwent comprehensive neuropsychological assessment (including Beck Depression Inventory, BDI), brain magnetic resonance imaging and levodopa challenge test. Non motor symptoms were assessed with the use of Non-Motor Symptoms Scale (NMSS), Parkinson's Disease Sleep Scale (PDSS), Epworth Sleepiness Scale (ESS), Single-Question Screen for RBD (RBD1Q), Parkinson's Disease Quality of Life Questionnaire (PDQ-39). Patients who fulfilled criteria of International RLS Study Group for the diagnosis of RLS were additionally examined with International RLS Study Group Rating Scale (IRLS). Patients were 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 post DBS programming. The first nights were considered to be adaptation nights and the obtained data were not analyzed, except for 2 patients whose recordings from the second nights were not valid due to the technical issues. All PSG studies were conducted in the sleep laboratory in the psychiatry clinic by a PSG technician and scored by a physician certified in sleep medicine (Polish Sleep Research Society Certificate). During the PSG recordings we used 2 EOG channels, 6 EEG channels (F3-A2, F4-A1, C3A2, C4-A1, O1-A2, O2-A), 3 EMG channels, 2 limb movement channels, 1 airflow channel, 1 ECG channel and 1 oximetry channel. DBS programming was performed at a median of 7 weeks post DBS implantation. The follow-up outpatient evaluations were performed 6 months and 12 months following DBS programming. We used the Shapiro–Wilk test to check whether the data followed normal distribution, then parametric (*t*-test) and non-parametric (Wilcoxon signed-rank and Mann–Whitney–Wilcoxon) tests 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 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 non-motor 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 [6–11]. 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 [10], 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,

Table 1 – The details of the subjects' characteristics compiled with PSG data.

Pt	Age	Sex	LED	TS (min) (pre/post)	SE (%) (pre/post)	WASO (min) (pre/post)	N1 (min) (pre/post)	N2 (min) (pre/post)	N3 (min) (pre/post)	R (min) (pre/post)
1	45	M	1620/1195	440/341	91.7/70.9	29.5/129.5	17.5/105	271.5/181.5	25/4.5	126/50
2	64	F	720/620	302.5/277.5	62.9/57.9	169/190.5	4/23	189/122	39.5/40	66/90.5
3	68	M	2275/1515	302.5/150	63/31.3	170.5/329.5	14.5/19	206.5/51.5	33/78	48.5/1.5
4	63	F	1200/990	329.5/182	68.6/38	133.5/279	10.5/38	195/59	92/74.5	32/8.5
5	58	M	2650/2750	360.5/217	75.1/45.1	114.5/248.5	10.5/93.5	248/93	22/2.5	80/28
6	64	F	1015/840	387.5/402.5	80.6/83.9	82.5/75	39.5/48	255.5/202	17/3.5	75.5/149
7	66	M	1540/1390	244.5/230	50.7/47.9	217/218.5	17/55	200/167.5	0/0.5	27.5/7
8	51	F	670/380	365/271.5	76/56.5	103.5/198.5	46.5/112.5	235.5/101.5	32.5/16.5	44/41
9	50	F	1670/640	326/177	67.8/51.2	145.5/161	20.5/32	250.5/104.5	15.5/25.5	39/15
10	59	F	750/590	366.5/201	76.4/41.9	76.5/232.5	25/41	262/101.5	64.5/46	15/11.5

F – female; M – male; LED – levodopa equivalent dose before surgery and 6 months after DBS programming; pre/post – results from preoperative polysomnography and postpoperative polysomnography; PT – patient; TS – total sleep time; SE – sleep efficiency; WASO – wakefulness after sleep onset.

Table 2 – The detailed results from the preoperative and follow-up polysomnographic recordings, non-motor and motor symptoms scales. The initial evaluation was performed at a median of 1.1 week before surgery and the follow-up evaluation at a median of 6.2 months post DBS programming.

Parameters	Preoperative evaluation, median (range)	Follow-up evaluation, median (range)	Statistics
Total sleep time (min)	345.0 (244.5–440.0)	223.5 (150.0–402.5)	$p = 0.001$[a]
Sleep efficiency (%)	71.8 (50.7–91.7)	49.5 (31.3–83.9)	$p = 0.02$
WASO (min)	124.0 (29.5–217.0)	208.5 (75.0–329.5)	$p = 0.004$[a]
Sleep latency (min)	10.5 (5.0–37.0)	13.2 (0.5–46.5)	NS
REM sleep latency (min)	105.2 (21.5–289.5)	110.0 (4.5–346.0)	NS
N1 (min)	17.2 (4.0–46.5)	44.5 (19.0–112.5)	$p = 0.01$[a]
N2 (min)	241.8 (189.0–271.5)	103.0 (51.5–202.0)	$p = 0.00001$[a]
N3 (min)	28.8 (0.0–92.0)	21.0 (0.5–78.0)	NS
R (min)	46.2 (15.0–126.0)	21.5 (1.5–149.0)	NS
Arousal index	17.9 (11.2–47.6)	20.1 (8.9–38.4)	NS
PLMI	0.5 (0.0–67.8)	0.0 (0.0–65.6)	NS
Apnea–hypopnea index	6.0 (0.0–36.6)	0.0 (0.0–1.1)	NS
RBD	0	0	NS
NMSS	55.5 (23.0–106.0)	34.5 (14.0–73.0)	$p = 0.017$[b]
PDSS	84.85(57.20–127.40)	95.95 (62.70–142.70)	NS
ESS	9.5(1.0–23.0)	7.0 (1.0–19.0)	NS
IRLSS[c]	25 (19–29)	18 (9–26)	NS
PDQ39	60.5 (29.0–99.0)	46.5 (13.0–57.0)	$p = 0.034$[a]
BDI	7.5 (3.0–16.0)	4.5 (0.0–15.0)	NS
UPDRS II	18.00 (11.00–26.00)	12.00 (0.00–19.00)	$p = 0.037$[b]
UPDRS III[d]	17.5 (5.0–34.0)	16.00 (7.00–26.00)	NS
UPDRS IV	8.00 (9.00–13.00)	5.0 (2.00–9.00)	$p = 0.0096$[b]

[a] Paired t-test.
[b] Mann–Whitney–Wilcoxon test.
[c] IRLSS was done in patients who fulfilled criteria of International RLS Study Group for the diagnosis of RLS.
[d] "On-state" scores; BDI – Beck Depression Inventory, ESS – Epworth Sleepiness Scale ESS, IRLSS – International RLS Study Group Rating Scale, NMSS – Non-Motor Symptoms Scale, NS – not statistically significant, PDSS – Parkinson's Disease Sleep Scale, PDQ39 – Parkinson's Disease Quality of Life Questionnaire, PLMI – periodic limb movements index, RBD1Q – Single-Question Screen for RBD, UPDRS – Unified Parkinson's disease rating scale, UPSIT – University of Pennsylvania Smell Identification Test, RBD – REM sleep behavior disorder, WASO – wakefulness after sleep onset.

contrary to the previous studies, we noted deterioration of sleep on the follow-up PSG evaluation. We found a decrease in the total sleep time and duration of the stage N2 with prolongation of the lightest sleep stage N1. We also detected an increase in duration of WASO. Compared to the previous studies, we observed an improvement of periodic limb movements index, however, this change was not statistically significant.

We did not detect any impact of DBS-STN on subjective severity of restless legs syndrome in our group of patients, whereas the data from previous studies are inconsistent, some reporting improvement and others even deterioration of RLS [10]. At the initial evaluation 6 patients complained of typical RBD symptoms and after DBS-STN the symptoms subsided in one of these patients, but at the same time appeared in 3 other patients. At the end of the study 8 patients reported such symptoms, however, RBD was not observed in any patient during PSG evaluations. In the majority of the previous studies RBD remained unchanged, however, Nishida et al. demonstrated restoration of the normal pattern of REM sleep [11].

Table 3 – The summary of the previous studies including most important findings.

Study	Number of patients	Mean age (years)	Mean disease duration (years)	Increased parameters	Unchanged parameters	Decreased parameters
Arnulf et al.	10[a]	Range of age: 40–60	NA	Sleep efficiency; total sleep time; N2 sleep; nocturnal motor symptoms	Number of awakenings; PLMS; RLS; RBD	WASO; axial dystonia during the night and early morning dystonia
Iranzo et al.	11	63.6 ± 7.8	17.3 ± 9.1	Number of body position changes; the longest period of continuous sleep	PLMS, RBD	arousal index
Cicolin et al.	5	63.8 ± 3.3	13.8 ± 4.9	Sleep efficiency; total sleep time; the percentage of stage 3–4 NREM sleep; the longest period of uninterrupted sleep	RBD, PLMS	WASO, REM latency
Monaca et al.	10	57.4 ± 5.2	12.1 ± 2.6	Total sleep time, sleep efficiency, deep slow-wave sleep and paradoxical sleep	Number of awakenings during sleep	
Nishida at al.	10	57.5 ± 9.8	12.3 ± 2.7	General sleep architecture; slow-wave sleep and normal REM sleep time;		WASO; REM sleep without atonia
Baumann-Vogel et al.	50	61 ± 10	12 ± 5	Total sleep time, sleep efficiency, N3 sleep;	Sleep latency; the duration of N1, N2, and REM sleep; awakening index; body position changes; awakening index; apnea–hypopnea index; RLS, REM sleep without atonia	WASO; REM sleep latency, PLMS

[a] Only patients with severe akinetic idiopathic PD and chronic insomnia before surgery; NA – not available, PD – Parkinson's disease, PLMS – periodic limb movement disorder, RBD – REM sleep behavior disorder, RLS – restless legs syndrome, RWA – REM without atonia, WASO – wakefulness after sleep onset.

As expected we confirmed the relationships between severity of subjective sleep disturbances, other non-motor symptoms and quality of life. We found a positive correlation between subjective sleep disturbances and the general perception of severity of non-motor symptoms. We also detected a negative correlation between severity of motor symptoms and the objective quality of sleep.

There have been several hypotheses regarding the mechanism of DBS-STN impact on sleep in PD. Sleep could be improved indirectly by alleviation of nocturnal motor symptoms, reduction in doses of antiparkinsonian medications, and directly by influencing the sleep/wakefulness regulatory centers [12]. The discrepancy between our results and the results from the six previous studies are more than expected and difficult to explain. Most of these studies used different methodologies and study designs, thus making it challenging to compare the results. The age and disease duration of our patients were generally similar to that in previous studies. Antiparkinsonian medications, especially levodopa, amantadine and selegiline may increase sleep fragmentation and induce insomnia. The data on medications that patients were taking during the previous studies are limited and the most detailed report is given in the study by Baumann-Vogel et al. [10]. Compared to this study our patients were taking significantly higher doses of medications. In our study on initial evaluation the levodopa equivalent dose (LED) was 1411 ± 673 mg and total levodopa dose was 1155 ± 694 mg, on follow up 1091 ± 690 mg and 825 ± 790 mg, whereas Baumann-Vogel et al. reported 1025 ± 480, 793 ± 450, 369 ± 376 and 309 ± 342, respectively. The same five patients (50%) were administered amantadine throughout the study compared to only 18% of patients before DBS and none after DBS in the study by Baumann-Vogel et al. Two patients were on selegiline in our study, however, there is no information about the intake of this medication in the previous studies. We did not find any correlation between the medication type and subjective and objective sleep parameters, possibly due to the small size of our group.

The discrepancy between subjective sleep measures along with PDQ39 improvement and objective deterioration of PSG parameters in our group remains unclear. It could be partially explained by the observed improvement in mood, as assessed by BDI, however, that difference was not statistically significant. Other factors that could have contributed to better perceived sleep quality were increase in nocturnal mobility (UPDRS part II question number 12, $p = 0.034$) and alleviation of complications of dopaminergic therapy (UPDRS part IV, $p = 0.0096$). Autonomic dysfunction symptoms, like nocturia, may also worsen sleep, however, we did not detect any relevant change in that domain. Finally, the placebo effect cannot be excluded.

5. Future directions

In summary, 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. These are the preliminary results of the first 10 patients included in our study and these findings will be verified on a bigger group of patients.

Ethical statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Author contributions

J.D., M.S., A.K., K.G., W.L., P.W., E.J.S. and J.S. worked on the manuscript.

Conflict of interest

None declared.

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