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A pilot study assessing the effects of pallidal deep brain stimulation on sleep quality and polysomnography in Parkinson's patients

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Abstract

Objective—Deep Brain Stimulation (DBS) is an established adjunctive surgical intervention to treat poorly controlled motor symptoms in Parkinson's disease (PD). Both surgical targets (the subthalamic nucleus and globus pallidus) have proven equally efficacious in treating motor symptoms but unique differences may exist in effects on nonmotor symptoms. Sleep dysfunction, a common disabling symptom in PD, has only been examined directly in the subthalamic target, demonstrating some beneficial changes in sleep quality. We aimed to explore sleep changes after pallidal stimulation; hypothesizing similar benefits would be seen.

Methods—We performed a prospective nonblinded clinical trial evaluating sleep in five PD patients already slated for pallidal DBS pre and six months post implantation using validated sleep surveys and polysomnograms (PSGs). Surveys included the Epworth sleepiness scale, Parkinson's disease sleep scale, Insomnia severity index, and RLS severity scale.

Results—Most patients had notable improvements in sleep quality as measured by PSG metrics such as sleep efficiency and latency to sleep but they did not reach statistical significance. Most surveys reflected an improvement as well with the Insomnia severity index scale showing the most promising trend post pallidal DBS (14.4 ± 7.02 vs. 9.0 ± 2.55 ; $p=0.07$).

Conclusion—In this small pilot trial, pallidal DBS failed to demonstrate statistically significant improvements in sleep metrics post implantation but did reveal improving trends in several PSG measures including sleep efficiency and latency to sleep onset as well as sleep survey scores. A

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larger, blinded clinical trial is needed to more definitively determine whether pallidal DBS may benefit sleep.

Keywords

Parkinson's disease; Deep Brain Stimulation; globus pallidus; sleep

Introduction

Parkinson's disease (PD) is a debilitating and progressive neurodegenerative condition classically managed by medications that augment the dopaminergic pathway. As the disease advances, alternative options geared towards providing more continuous therapeutic benefit such as Deep Brain Stimulation (DBS) are becoming more commonly used as adjunctive treatments to help manage long-term complications (e.g. dyskinesias and motor fluctuations) of the classic medicinal therapies. There are two accepted anatomical targets (the globus pallidus interna (GPi) and subthalamic nucleus (STN)) used in DBS to treat PD. These two targets have proven to be equally efficacious in treating the overall diagnostic motor features of PD in large comparative trials (1–2). However, previous studies also suggest potential differences in the targets in terms of post-surgical neuropsychiatric measures, medication reduction, and fall risk among others (1, 3–4). Data are still lacking to reliably tailor the target to an individual patient. One possible area, which may help clinicians decide on the target, is the nonmotor features of Parkinson's disease. These are not typically modified by PD medications but are highly disabling for patients. There are some limited studies that show that DBS may in fact benefit some nonmotor features (5–6).

Sleep disruption is very common and problematic in PD with estimates that 74–98% of PD patients suffer from some type of sleep problem (7). This can include REM sleep behavior disorder (RBD), restless legs syndrome (RLS), wearing off at night, nocturia, insomnia, sleep fragmentation, vivid dreams and nightmares, and excessive daytime somnolence among others (7–12). Large clinical DBS studies have incidentally noted some benefits on sleep (13–14). There have also been some studies of much smaller sample size designed specifically to look at sleep changes post-DBS using both sleep measurement scales and polysomnograms (PSG) (14–22). Consistently, these have shown benefits in sleep quality but have failed to show objective changes in sleep architecture on the PSG. Unfortunately, all these studies involve subjects who had undergone STN–DBS. There are very little data from the GPi target, other than larger quality of life surveys, which have incidentally found a benefit as well (23–25).

We investigated the potential benefit of pallidal DBS on sleep in PD patients using a sample size similar to those studies done in the STN target. Using both sleep scales and PSGs, our aim was to better understand the effects of pallidal DBS on sleep in PD patients.

Materials and Methods

This pilot study was an IRB approved prospective, non-blinded clinical trial designed to further evaluate changes in sleep pre and post GPi-DBS for PD. Study participants were selected from PD patients (defined by expert opinion and the UK brain bank criteria) at

Vanderbilt University Medical Center already slated for pallidal DBS. During the study period, every eligible candidate who met inclusion/exclusion criteria was approached for entry into the study and provided written consent if they wanted to proceed. Our center evaluates candidacy and selects anatomical target for impending DBS cases at a monthly conference attended by neurologists, neurosurgeons, physical therapists and neuropsychiatrists. There are no set criteria for selecting DBS target but our center places particular emphasis on depression, postural instability, lower levels of medication, and impaired verbal fluency as reasons to proceed with the GPi target. Symptoms of sleep disruption were not discussed at these conferences.

After the conference and target selection, potential cases were screened with the STOP-BANG survey in attempts to identify and exclude patients with possible obstructive sleep apnea (OSA) immediately before enrollment in the study over concerns it could be a confounding variable (26–27). The correlation of OSA with PD is still highly debatable (28–32). Further, OSA and the apnea-hypopnea index have been shown in limited cases to improve after DBS which could certainly reflect improved sleep quality on its own (33). Given this patient population already scores high on the STOP-BANG due to older age, current symptoms of daytime sleepiness and male predominance, and the fact the STOP-BANG has been shown to have low specificity in PD, we used a cut off of 5 as an exclusion (34). If patients had a body mass index greater than 35 kg/m² with a history of loud snoring or nocturnal apneic events, they were also automatically excluded. Further exclusion criteria included the inability by the patient to accurately respond to selected sleep scales, deficits in cognition at the level of mild cognitive impairment or lower as defined by neurocognitive testing, and pregnancy (female patients were either post-menopausal or received a pregnancy test). Finally, after this screening, if patients had OSA on the preoperative PSG, they were removed from further study evaluations as well. Only one participant passed screening with the STOP-BANG yet had evidence of OSA on their preoperative PSG necessitating removal.

Study participants were evaluated preoperatively and then six months post-operatively. At the time of the post-operative visit, Parkinson's drugs had been titrated as clinically able and DBS settings optimized. DBS lead placement in the GPi was also confirmed using postoperative CT imaging and a functional atlas in a normalized space. Pre-operative and post-operative assessments for this study were performed at the Vanderbilt Clinical Research Center Sleep Core, and involved an overnight PSG and assessment of validated sleep scales. These sleep scales included the Epworth sleepiness scale (ESS), the Parkinson's disease sleep scale (PDSS), the Insomnia severity index (ISI), and the RLS severity scale (35). Restless legs syndrome (RLS) was determined by accepted diagnostic criteria (36). The PI administered all scales.

A trained sleep technologist performed the overnight PSG using standard protocols. The PSG was performed in digital video format consisting of six electroencephalogram channels (F3,F4,C3,C4,O1,O2); three chin electromyogram leads; two electrooculogram leads; two electrocardiogram leads; thermocouples and nasal pressure cannulas measuring airflow at the nose and mouth; and bilateral surface electromyogram on the legs. Oxyhemoglobin saturation was monitored by pulse oximetry. The tracing was scored in 30-second epochs. The scoring of sleep and all associated events were performed in accordance with the

recommended Standards and Specifications as outlined in the *AASM Manual for the Scoring of Sleep and Associated Events* (37). Apneas were scored if there was a > 90% decrement in the thermistor for at least 10 seconds and hypopneas were scored if there was a 50–90% decrement in the nasal pressure transducer for at least 10 seconds with concurrent oxyhemoglobin desaturation of 4% or greater based on the Medicare criteria for scoring hypopneas.

On the PSG, specific focus was directed at sleep architecture, the periodic limb movement (PLM) index, REM sleep without atonia, sleep efficiency, sleep onset latency, the arousal index, wake after sleep onset (WASO) and scoring of respiratory events. A trained sleep technologist performed the overnight PSG using standard protocols and staged it according to standard guidelines (38). In attempts to avoid any convoluting artifact on EMG and EEG from DBS, the montage F3 to C4, F4 to C3, and O1 to O2 was used as seen in prior published DBS sleep studies (16, 18). This was compared to the standard sleep montage for accuracy. As with prior DBS protocols, the high frequency filter was also decreased to 15 Hz in the EEG channels and to 35 Hz in the EMG channels to avoid stimulation induced artifact as well. OSA was defined as daytime sleepiness and an apnea hypopnea index of 5 or greater. Final scoring of the sleep studies was performed by Dr. Bagai, a neurologist specializing in sleep medicine and well experienced in reading PSGs.

Descriptive statistics were used when assessing general variables in our sample including gender, age, medical comorbidities, time since diagnosis of PD, levodopa equivalent daily dose (LEDD) and degree of dopamine agonist use (LEDD DA). When comparing sleep metrics and other variables pre and post implantation, we performed a nonparametric paired t test, the Wilcoxon signed-rank test, using SPSS® 22.0.

Results

Seven patients met initial inclusion criteria and underwent preoperative assessments. One patient was found to have OSA on the preoperative sleep study and was removed from the trial. A second patient had a surgical complication requiring discharge from the study. Of the five patients who had pre and postoperative assessments, 60% (3/5) were male and all were Caucasian. Basic demographic and medication information is documented in Table 1. This patient population was typical of most DBS populations with an average age of 62, Hoehn and Yahr off medication of 3.4 (median 3), and an average disease duration at time of surgery of 9.8 years. Preoperatively, all patients were taking a combination of at least a dopamine agonist and L-dopa. They demonstrated a marked response to dopaminergic medication with a 47% improvement on the UPDRS on/off medication, supporting a diagnosis of PD.

Postoperatively, all patients were able to decrease medication with a statistically significant drop in total LEDD from 1537.40 to 1129.3 ($p=0.04$). In regards to dopamine agonist use, there was no significant change in dose post-operatively ($p=0.18$). One patient was able to completely discontinue their dopamine agonist, another to decrease by 25%, and the others were unchanged. We correlated the percent change in LEDD with sleep metrics. Only ESS score (-0.60) and ISI score (-0.92) had any sign of a correlation with Pearson Correlation

coefficients above 0.5. There was no correlation seen with PSG metrics. When we correlated the percent change in LEDD DA with sleep metrics, ESS score (-0.58), sleep efficiency (-0.65), and sleep latency (0.55) had some modest correlation with Pearson Correlation coefficients slightly above 0.5.

In this sample, the sleep scales showed encouraging trends towards improved sleep quality post-DBS but the changes did not reach statistical significance (Table 2). The ESS was the only scale that reflected a negative change following surgery but this was minimal and not thought to be clinically meaningful (preoperative 10.6 ± 4.51 ; postoperative 11 ± 4.74). On the ESS, scores of 0–10 are considered normal while scores greater than 10 are considered indicative of daytime sleepiness. The ISI changed from an average score of 14.4 ± 7.02 to 9.0 ± 2.55 , bordering on a statistically significant change that moved from scores concerning for insomnia to nearly normal thresholds ($p=0.07$) which, given our small sample, is notable. With this scale, 0–7 is normal while 8–14 raises concerns of insomnia. The PDSS also improved (pre: 90.24 ± 20.44 , post: 106.42 ± 17.40 ; $p=0.14$). In the PDSS, there are no set cut offs but higher scores correspond to less sleep dysfunction. Here, too, while nonsignificant, a 16 point improvement likely indicates a clinically meaningful improvement. Finally, while only 2/5 patients met all four diagnostic criteria for RLS, the RLS severity score dropped from 9.8 ± 13.97 to 3.4 ± 4.67 . Scores from 0–10 are all considered mild.

There was no significant change in sleep metrics and morphology on the PSG after pallidal DBS (Table 2). There was also very little difference seen between the AASM and DBS montages with sleep staging. Given that, results described here will reference the DBS montage. Despite the lack of statistical significance, there were some promising trends in the PSG metrics with some robust changes post-surgery. Sleep efficiency improved from 59.2% to 72.6% post implantation ($p=0.27$). Wake after sleep onset (114.6 vs. 79.6 minutes; $p=0.23$); sleep latency (60 vs. 28.4 minutes; $p=0.23$), and REM latency (223 vs. 95.5 minutes; $p=0.11$) all improved, decreasing considerably in every instance post-surgery. With sleep stages post-implantation, there was a notable increase in N2 (NREM stage II) and REM sleep with a corresponding decrease in N1 (NREM stage I) sleep (Figure 1). Average N3 % was low at $4.14\% \pm 6.55$ pre-surgery but reduced to an average of 0% post-surgery. Polysomnography of adults and elderly have shown the percent of slow wave sleep in individuals with age greater than 60 (which is representative of our population) to be in the range of $5.1\% \pm 5.7$ (mean + SD) (39). The PLM index (32 vs. 6.82; $p=0.27$) and arousal indexes (37 vs. 14; $p=0.35$) also showed improvement post-implantation. Finally, both during pre and post-surgery PSG's, no REM sleep without atonia was observed. The magnitude of all these PSG changes was compared with that seen in prior STN studies and was found to be similar (Table 4).

Table 3 details out information on individual patients. No subject appeared as a substantial outlier to skew statistical results. Subjects 3–5 overall had more improvements on most sleep metrics while this was less profound in subjects 1 and 2. However, of those subjects with less profound change, subject 2 had consistently some of the best preoperative baseline sleep scores making opportunities to perceive improvement likely limited by ceiling effects (i.e. very little room for improvement post-surgery). ESS scores were unchanged to slightly worse in most subjects (exception subject 4) while other survey scores reflected mostly

positive change including RLS scores in those with RLS. On the PSG, sleep efficiency and WASO notably improved in subjects 3–5, sleep latency improved in all subjects but subject 1, and REM latency improved in all subjects but subject 3. There was some variability to the changes in sleep architecture post-surgery. In most patients, N1 sleep decreased (exception of subject 2), N2 increased (exception of subject 1 and 2) and REM sleep increased (exception of subject 2 and 3).

Discussion

This pilot study was a nonblinded, prospective clinical trial designed to evaluate the benefit of GPi-DBS on sleep in Parkinson's disease. Both the sleep surveys and PSG data overall demonstrated positive trends after pallidal stimulation, often with robust changes that appeared clinically significant. Despite these overall positive trends in our study metrics, there was not a statistically significant change in either the survey scores or the PSG metrics post-surgery as seen in prior studies using the STN target.

Specifically, in regards to the surveys, there were improved trends noted in the ISI and PDSS scores in the post-DBS surveys. The improved trends noted on the ISI may be a reflection of the improvements seen in the PSG metrics. There was also an improvement of the RLS severity rating in the 2 patients who met RLS criteria initially. Interestingly, there was an improvement in the periodic leg movements (PLM) index noted on the PSG as well, although it did not reach statistical significance. The ESS was the only sleep scale that did not improve, in fact demonstrating some slight worsening overall. The minimal change is considered clinically not meaningful, but the reason for this worsening is unclear in view of the changes in the other scales and PSG metrics. In both patients with worse ESS scores, the ISI and PDSS scores still improved.

In regards to the PSG studies, there were trends for improved sleep efficiency and arousal index, decreased sleep latency and reduced wake after sleep onset. All of these measures reflect improvement in sleep quantity and can clinically result in improvement in insomnia symptoms. There was reduction in the percent amount of N1 sleep noted in our patients' post-DBS. In addition, there was an increase in N2 and REM sleep duration noted on the PSGs done post-DBS. N1 (NREM stage 1) sleep reflects the transition stage from wakefulness to sleep and reflects the lighter stage of sleep whereas N2/N3 sleep are the deeper stages of NREM sleep, and reflect sleep continuity. N3 is often not detected in elderly individuals, especially males, and hence the change seen in this study is less clinically meaningful (39). Although none of these variables reached statistical significance, the combination of the results reflects a trend towards more normative values for the >60 year old age group (40).

Several studies, also of limited sample size (n=5–11), have used polysomnograms to evaluate sleep on/off STN-DBS (7). These have consistently shown benefits in sleep quality measures including total sleep time, sleep efficiency and/or WASO, but inconsistent changes in sleep stages. Arnulf et al demonstrated statistically significant decreased WASO, decreased early morning dystonia and increased sleep efficiency in a study looking at patients on/off stimulation (15). Iranzo et al and Monaca et al found similar findings of a

subjective improvement in sleep quality and increased continuous sleep time in their studies pre and post STN-DBS (16–17). There were other select findings as well of decreased nocturnal mobility and increased sleep efficiency. Finally, Cicolin et al reported a study of five patients and found significantly decreased WASO, increased sleep efficiency, and decreased REM latency (18). The magnitude of these changes again compare favorably with that seen in our study (Table 4). In several instances, the changes witnessed with pallidal stimulation are more robust. There are other studies investigating the effects of STN-DBS that have used sleep rating scales done at varying study intervals, up to 24 months. These scales have included the Parkinson's Sleep Scale, Epworth, Pittsburgh Sleep Quality Index and the UPDRS (Part IV). Consistently, there have been findings of improved sleep quality and increased sleep time as with the studies using polysomnograms (14, 19–22).

Data on GPi-DBS effects on sleep are very limited. There are no known studies using primary sleep measures like the present study to assess sleep in GPi DBS. Peto et al looked at an overall quality of life scale in GPi-DBS and noted that 6/10 subjects had a subjective improvement in daytime sleepiness (23). Volkmann et al looked at 20 patients using the Sickness Impact Profile questionnaire and found improvement in sleep quality (24). There are also some limited data on pallidotomy perhaps improving sleep (25).

This study has several limitations. It would be hard to use this data to make meaningful conclusions on the GPi target's effects on sleep. The sample size in this study is small and was likely underpowered to demonstrate true statistical differences. As this was a pilot trial, sample size calculations were determined using data from the STN sleep studies. A post-hoc sample size calculation argues that, if we were planning a study using the current data and sleep efficiency as our primary outcome measure with a standard deviation of about 20–30 and difference in the mean response of matched pairs of 20%, then we would need to study 10–20 pairs of subjects to be able to reject the null hypothesis that this response difference is zero with probability (power) 0.8 and an alpha of 0.05. Despite this limitation in our current study, the prior STN studies using PSGs were still statistically significant even at small sample sizes similar to our own. Given some notable improvements in sleep metrics in our study despite the small sample size, this very likely reflects the fact that the effect size needed to see a change in sleep post pallidal stimulation is simply larger than that in the STN target. Another limitation is that patients in our study were not randomized to the GPi in a blinded fashion. The sample was skewed given our current selection criteria for the GPi target that include evidence of depression, lower LEDD levels, higher risk of falls, and impaired verbal fluency. Several of these criteria such as depression and medication can impact sleep and their impacts could not be fully elucidated. For this pilot trial, we felt it unethical to blindly randomize patients to pallidal stimulation given the current information on target selection we use at our center and, in turn, lack of information on sleep. Given we excluded OSA patients, our sample was also unique compared to some other DBS sleep studies, perhaps limiting comparisons, but we felt this exclusion important over concerns effects on OSA might confound objective and subjective changes in sleep quality. Finally, as evidenced by some possible correlation with medication percent change on some sleep metrics, there could be a variety of predictors for why a PD patient's sleep may or may not respond to pallidal stimulation such as medications, phenotypic characteristics, age, gender, or other unknowns. Dyskinesias, for example, were not objectively measured in this cohort

but their presence and potential improvement post DBS could have an effect on sleep latency, RLS and other sleep metrics. None of the patients enrolled in this study demonstrated significant dyskinesias but certain centers do favor the GPi target for patients with prominent dyskinesia. All of these potential confounders would need more study in a larger randomized trial.

Conclusion

This pilot study provided preliminary data on the effects of pallidal stimulation on Parkinson's disease patients. The overall changes in sleep metrics post-surgery were notable and likely clinically important for individual patients. However, despite these positive trends, this study failed to demonstrate a statistically significant benefit on scores with sleep surveys or PSG metrics. The study was limited by small sample size and underpowered due to its pilot nature. However, the sample was comparable to those reported in prior STN-DBS sleep studies, which did demonstrate statistical significance. Consequently, it would be premature to conclude that GPi DBS does not benefit sleep. Ultimately, further investigations using larger, preferably blinded, trials both solely with GPi-DBS and comparatively with STN-DBS are needed to fully elucidate the differences in the effects on sleep after DBS. This is important if there are indeed differences in targets as DBS centers seek to tailor the therapy to individual patients.

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Figure 1.

Legend: Sleep stages pre and post Deep Brain Stimulation. Legend: DBS=Deep Brain Stimulation, N1=NREM stage 1 sleep (sleep wake transition), N2=NREM stage 2 sleep, N3=NREM stage 3 sleep (deep sleep), REM=rapid eye movement (final sleep stage)

Table 1

Basic demographic and clinical information of study patients

	PreOp	Postop	P value
Age (years)	62 (7.18)		
Disease Duration (years)	9.8 (3.96)		
Ht (cm)	168.66 (11.16)	168.15 (9.74)	0.66
Wt (kg)	76.13 (22.24)	72.47 (12.61)	0.69
BMI	26.24 (4.40)	25.42 (2.20)	0.69
LEDD agonist	462 (233.92)	312 (265.46)	0.18
LEDD Total	1537.40 (585.37)	1129.30 (425.79)	0.04*
Hoehn and Yahr (off)	3.4 (0.55)		
UPDRS Part III (off)	39.8 (12.97)		
UPDRS Part III (on)	21.2 (6.87)		

Legend: Ht=Height, Wt=Weight, BMI=Body mass index, LEDD agonist=Levodopa equivalent daily dose of dopamine agonists, LEDD=Total levodopa equivalent daily dose, off=off medication, on=on medication, UPDRS Part III=United Parkinson's disease Rating Scale. Values correspond to means with standard deviation in parentheses.

Table 2

Sleep measures pre and post DBS

	PreOperative Testing (T1)	Postoperative Testing (T2)	P value
Stop Bang	2.4 (0.89)	2.6 (1.14)	0.32
Epworth Sleep Scale	10.6 (4.51)	11 (4.74)	0.85
Insomnia Severity Index	14.4 (7.02)	9 (2.55)	0.07
Parkinson's Disease Sleep Scale	90.24 (20.44)	106.42 (17.40)	0.14
Restless Legs Syndrome Severity Scale	9.8 (13.97)	3.4 (4.67)	--
Total Recorded Time (min)	452.20 (64.60)	426.20 (51.98)	0.35
Apnea Hypopnea Index	2.26 (0.73)	2.32 (1.26)	0.79
Total Sleep Time (min)	274.80 (166.14)	311.60 (89.97)	0.69
Sleep Efficiency (%)	59.2% (32.31)	72.6% (14.57)	0.27
WASO (min)	114.6 (77.84)	79.6 (48.34)	0.23
Sleep Latency (min)	60 (76.17)	28.4 (39.05)	0.23
REM latency (min)	223 (90.20)	95.5 (13.70)	0.11
Stage N1 (%)	33.5% (34.47)	12.66% (8.22)	0.14
Stage N2 (%)	59.3% (27.86)	78.08 (8.29)	0.14
Stage N3 (%)	4.14% (6.55)	0	0.18
REM (%)	4.56% (4.60)	9.26% (11.13)	0.5
Stage N1 (min)	51.6 (23.32)	36.4 (16.20)	0.14
Stage N2 (min)	196.6 (164.94)	247.6 (91.2)	0.35
Stage N3 (min)	13.2 (23.39)	0	0.18
REM (min)	14 (14.54)	28.6 (34.83)	0.35
PLM Index	32 (39.13)	6.82 (9.77)	0.27
Arousal Index	37 (33.01)	14 (17.82)	0.35

Legend: T1=Time 1; T2= Time 2; WASO= Wake After Sleep Onset; PLM=Periodic Limb Movement. Values correspond to means with standard deviation in parentheses. The Restless Legs Syndrome Severity Scale did not have a p value because sample size was too small (n=2).

Table 3

Individual Data

	Subject 1	Subject 2	Subject 3	Subject 4	Subject 5
Hoehn and Yahr	3	4	3	3	4
UPDRS preop (off/on)	20/15	46/25	35/15	44/20	54/31
LEDD total (pre/post)	1000/775	960/610	1647/1447.5	1700/1600	2380/1214
LEDD agonist (pre/post)	600/450	60/60	450/450	600/600	600/0
Stop Bang (pre/post)	1/1	3/3	3/3	2/2	3/4
ESS (pre/post)	6/5	7/7	13/16	17/13	10/14
ISI (pre/post)	16/12	5/5	18/10	23/9	10/9
PDSS (pre/post)	110.8/105.9	110.5/126.5	90/93	72.6/120.8	67.3/85.9
RLS Severity Scale (pre/post)	0/0	0/0	19/9	30/8	0/0
TRT (min) (pre/post)	399/387	543/486	415/376	498/404	406/478
Apnea Hypopnea Index (pre/post)	1.2/0.8	1.9/2.1	2.4/3.8	2.8/1.5	3.0/3.4
TST (min) (pre/post)	356/288	503/452	200/202	254/314	61/302
Sleep Efficiency (%) (pre/post)	89%/74%	93%/93%	48%/55%	51%/78%	15%/63%
WASO (min) (pre/post)	38/68	24/31	194/160	158/60	159/79
Sleep Latency (min) (pre/post)	4/28	16/2	16/9	78/8	186/96
REM latency (min) (pre/post)	306/100	269/112	99/-	218/80	-/90
Stage N1 (%) (pre/post)	14.3%/10.4%	6.3%/11.4%	44.4%/26.9%	13.2%/6%	89.3%/8.6%
Stage N2 (%) (pre/post)	70%/84.5%	88%/88%	45.1%/73.1%	75.4%/67.6%	18%/77.2%

	Subject 1	Subject 2	Subject 3	Subject 4	Subject 5
Stage N3 (%) (pre/post)	15%/0%	0%/0%	5.7%/0%	0%/0%	0%/0%
REM (%) (pre/post)	0.7%/5%	6%/0.7%	4.7%/0%	11.4%/26.4%	0%/14.2%
Stage N1 (min) (pre/post)	51/30	31/51	89/56	33/19	54/26
Stage N2 (min) (pre/post)	249/243	442/398	90/152	191/212	11/233
Stage N3 (min) (pre/post)	54/0	0/0	12/0	0/0	0/0
REM (min) (pre/post)	2/14	30/3	9/0	28/83	0/43
PLM Index (pre/post)	6/0	68/0	81/21.1	0/0	5/13
Arousal Index (pre/post)	7/10	22/45	47/0	19/5	90/10

Legend: UPDRS=United Parkinson’s disease Rating Scale Part III; LEDD=Levodopa daily equivalents; ESS=Epworth Sleep Scale; ISI=Insomnia Severity Index; PDSS=Parkinson’s disease Sleep Scale; RLS=Restless legs Syndrome; TRT=Total Recording Time; TST=Total Sleep time; WASO=Wake After Sleep Onset; PLM=Periodic Limb Movement. Numbers before and after the backslash correlate with pre/post operative values or on/off UPDRS scores.

Table 4

Change in sleep metrics post DBS

Study	Tolleson et al	Iranzo et al ¹⁶	Monaca et al ¹⁷	Cicolin et al ¹⁸	Arnulf et al ¹⁵
Sleep Efficiency %	+13.4	-6.1	+15.3	+60	+14.6
WASO (min)	-35	-11.8	-69	-49	-51
Sleep Latency (min)	-31.6	-22.6	-71.7	-58	-10
REM latency (min)	-127.5	--	--	-65	-20
Stage N1 (%)	-20.8	+2.2	-3.4	-2.8	+0.4
Stage N2 (%)	+18.8	-9.2	-8.8	-7.8	+5.4
Stage N3 (%)	-4.1	+6.7	+9.1	+8.3	-3.0
REM (%)	+4.7	+0.2	+2.6	+2.3	+1.9
PLM index	-25.2	+6.9	--	-7.1	--
Arousal Index	-23	-6.8	--	--	+1.3

Legend: WASO= Wake After Sleep Onset; PLM=Periodic Limb Movement. Values correspond to mean changes pre/post surgery or off/on stimulation.