Effects of implantation of a deep brain stimulation device on patient weight in Parkinson's disease and essential tremor

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OBJECTIVE Deep brain stimulation (DBS) is a well-established therapy for treating neurological movement disorders. Some patients who have received DBS therapy have noticed significant weight gain. Further investigation into correlations between patient characteristics and weight gain following DBS device implantation, which the authors here have done, will provide physicians with useful clinical information.

METHODS The authors performed a retrospective study of patients with Parkinson's disease (PD) and essential tremor (ET) who had received DBS therapy in the period from 2012 to 2017. Patient weights had been recorded preoperatively and at 3, 6, and 12 months postoperatively. These data were used to compare patient characteristics, including diagnosis, body mass index (BMI), sex, levodopa equivalent dose (LED), and change in Unified Parkinson's Disease Rating Scale (UPDRS) score. For PD patients, a quantile multivariate regression analysis was used to examine whether significant correlations existed between several of these patient characteristics, as well as age and weight gain following implantation.

RESULTS PD patients had gained a significant amount of weight at 3 months (mean [SE] 2.66 [0.428] kg, $p < 0.001$), 6 months (3.64 [0.492] kg, $p < 0.001$), and 12 months (4.18 [0.540] kg, $p < 0.001$) after DBS placement. Patients who had undergone subthalamic nucleus (STN) DBS device placement gained, on average, more weight than the patients with globus pallidus internus (GPi) placement at both 6 months (mean 2.558 [1.020] kg, $p = 0.01$) and 12 months (2.358 [1.130] kg, $p = 0.04$). BMI in the STN cohort was greater than that in the GPi cohort at 6 months (mean difference [SE] 2.60 [1.127] kg/m², $p = 0.02$) and at 12 months (2.36 [1.112] kg/m², $p = 0.04$). A reduction in LED was negatively correlated with weight change at 6 months ($r = -0.33$, $p < 0.001$) and 12 months ($r = -0.41$, $p < 0.001$). There was no weight gain correlated with DBS therapy for ET.

CONCLUSIONS PD patients experienced a significant change in weight over time after DBS therapy, whereas ET patients did not. PD patients with an STN target site experienced greater weight gain, on average, than those with a GPi target site. Furthermore, there was a significant increase in BMI at 6 and 12 months in patients with an STN target compared to that in patients with a GPi target. PD patients whose LED was reduced after DBS gained more weight at 6 and 12 months after surgery than the patients whose LED was kept at the same level or increased.

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KEYWORDS deep brain stimulation; essential tremor; Parkinson's disease; postoperative weight gain; stereotactic and functional neurosurgery

ABBREVIATIONS BMI = body mass index; DBS = deep brain stimulation; ET = essential tremor; GPi = globus pallidus internus; LED = levodopa equivalent dose; LID = levodopa-induced dyskinesia; PD = Parkinson's disease; STN = subthalamic nucleus; UPDRS = Unified Parkinson's Disease Rating Scale; VIM = ventral intermediate nucleus.

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BOTH Parkinson's disease (PD) and essential tremor (ET) are neurological movement disorders. Weight loss can occur during the natural course of either disease. Deep brain stimulation (DBS) uses stimulating electrodes that are implanted into the brain to generate high-frequency electrical pulses that modify the activity of neural conduction networks to help treat ET and motor symptoms of PD. Weight gain after DBS electrode placement in PD and dystonia patients has been reported.^{1,2} Alleviating hyperkinetic symptoms (e.g., tremor, dyskinesias) can lead to decreased daily energy expenditure, which may be the mechanism behind the observed weight gain, but other mechanisms, such as stimulation of the satiety centers of the thalamus, have been proposed as well. In this study, we quantified weight gain after DBS surgery and examined whether that weight gain correlated to variables such as the patient's disease (PD vs ET), electrode placement target (subthalamic nucleus [STN] vs globus pallidus internus [GPi]), body mass index (BMI), patient sex, patient age, reduction in levodopa equivalent dose (LED), and reduction in Unified Parkinson's Disease Rating Scale (UPDRS) score.

Methods

This study was approved by the St. Joseph's Hospital and Medical Center Institutional Review Board. We conducted a retrospective study of patients with PD and those with ET who had received DBS therapy in the period from 2012 to 2017. All patients with ET received ventral intermediate nucleus (VIM)-targeted DBS. All electrodes were implanted bilaterally on the procedure day and activated at a follow-up appointment.

In accordance with routine clinic protocol, weights were obtained preoperatively and at 3, 6, and 12 months postoperatively. Because of variability in the dates of follow-up appointments, there was a margin of ± 2 months for each of those time frames. Patient weight data were used to compare groups by disease, electrode placement target, BMI, sex, reduction in LED, age, and UPDRS score. BMI and LED were recorded preoperatively and at 6 months and 12 months postoperatively. The UPDRS score was collected preoperatively and postoperatively and compared with weight change at 12 months postoperatively.

Statistical Analysis

For PD, we first separated the patients by sex and DBS target (STN and GPi). We then ran a repeated-measures ANOVA with a Greenhouse-Geisser correction to determine the mean weight change, standard error, and statistical significance of the weight change at each of the postoperative time points (3, 6, and 12 months) compared to the preoperative weight for each of these categorical variables, including the uncategorized PD cohort as a whole. A similar procedure was used in presenting change in BMI, in which we used a repeated-measures ANOVA with a Greenhouse-Geisser correction to analyze the mean BMI change, standard error, and statistical significance of the BMI change at each of the postoperative time points (6 and 12 months) compared with the preoperative BMI for both the PD cohort as a whole and the PD patients strati-

fied by target. A post hoc Bonferroni adjustment was applied to all of these analyses to account for repeated measures. A Greenhouse-Geisser correction was used because Mauchly's test of sphericity was violated.

We then investigated the correlations between either sex or DBS target (STN vs GPi) and weight gain (calculated from preoperative weight) over the postoperative period (3, 6, and 12 months). For these comparisons, we used a mixed-factorial ANOVA with a Greenhouse-Geisser correction to determine the main effects of time on weight change, the effect of the variable sex or target on weight change, and the possible interaction of time and sex or target with weight change. We set up this ANOVA with weight changes at 3, 6, and 12 months as our dependent variables and then had either target (STN or GPi) or sex as our independent variable or our between-subjects variable. After running this analysis, we were able to determine the F value for the effect of time and either sex or target on weight change. Results are reported as $F(df_{\text{source}}, df_{\text{error}}) = F \text{ value}$. If there was a significant interaction, we followed up our ANOVA with post hoc tests of simple effect to determine the difference in weight change between either sex or target at each postoperative time point.

We performed a similar procedure as above for analyzing both BMI and LED over the postprocedural time measured. However, instead of using change in BMI or LED at 6 and 12 months postoperatively as our independent variable, we used the patient's BMI and LED preoperatively and at 6 and 12 months postoperatively as our independent variables. We wanted to determine whether there was a significant interaction between DBS target (STN vs GPi) and BMI or LED over the postoperative period (6 and 12 months postoperatively).

For PD, we also wanted to determine the statistical difference between preoperative and postoperative UPDRS scores. For this analysis, we ran a paired samples two-tailed t-test. Results are reported as the mean (standard error).

Furthermore, we ran a Pearson's correlation analysis to determine the relationship between change in UPDRS score and change from preoperative to postoperative weight at 12 months. Additionally, we used Pearson's correlation analysis to determine the relationship between the change in LED and postoperative weight at 6 and 12 months.

Finally, for the cohort of PD patients, we used a quantile regression analysis to determine the relationship between our variables—DBS target site, preprocedure BMI, patient sex, reduction in LED, and patient age—and weight change (kg) at 3, 6, and 12 months.

For ET patients, we stratified the cohort by sex. We ran a repeated-measures ANOVA to determine the mean weight change at each follow-up time (3, 6, and 12 months) compared with the preoperative weight for the entire ET cohort and the male and female patients with ET separately. We then performed a post hoc Bonferroni adjustment to account for repeated measures and a Greenhouse-Geisser correction for not meeting Mauchly's test of sphericity. The results are reported as the mean (standard error).

A p value < 0.05 was considered statistically significant for all data analyses. All analyses were completed using SPSS Statistics software (IBM Corp.).

Results

Parkinson's Disease

The PD cohort consisted of 70 men and 30 women. Among those patients, 67 received STN-targeted DBS, and 33 received GPi-targeted DBS. Patients with PD showed a mean (SE) weight gain of 2.66 (0.428) kg at the 3-month follow-up ($p < 0.001$), 3.64 (0.492) kg at the 6-month follow-up ($p < 0.001$), and 4.18 (0.540) kg at the 12-month follow-up ($p < 0.001$). In those patients, electrodes had been placed in either the STN or the GPi. Patients with STN DBS showed a mean weight gain of 2.95 (0.552) kg at the 3-month follow-up ($p < 0.001$), 4.49 (0.588) kg at the 6-month follow-up ($p < 0.001$), and 4.96 (0.678) kg at the 12-month follow-up ($p < 0.001$) as compared with their preprocedural weight (Table 1). Compared with the STN DBS patients, the GPi DBS patients experienced less weight gain overall, with a mean weight gain of 2.07 (0.654) kg at the 3-month follow-up ($p = 0.02$), 1.93 (0.830) kg at the 6-month follow-up ($p = 0.16$), and 2.60 (0.833) kg at the 12-month follow-up ($p = 0.02$).

In comparing the effect of STN versus GPi placement on weight change over the postoperative time, a mixed-factorial ANOVA with a Greenhouse-Geisser correction revealed that there was a significant effect of time and target on weight change ($F[1.79, 175.40] = 3.28, p = 0.045$). Post hoc testing of simple effects revealed that the results between DBS target and weight change were not statistically significant at 3 months postoperatively ($p = 0.34$). However, the difference was significant at 6 months (mean [SE] 2.558 [1.020], $p = 0.01$) and at 12 months (2.358 [1.130], $p = 0.04$); that is, patients who had undergone STN DBS device placement gained, on average, more weight than the patients with GPi placement at these follow-up times.

BMI (calculated as weight in kilograms divided by the square of height in meters) was measured preoperatively and at 6 and 12 months postoperatively. The patient's BMI following DBS device placement was then stratified by the DBS target (Table 2). At 6 months, BMI had increased by a mean (SE) 1.35 (0.183) kg/m² ($p < 0.001$), and at 12 months by 1.54 (0.197) kg/m² ($p < 0.001$). In comparing the effect of STN versus GPi target on BMI over the postoperative follow-up period, a mixed-factorial ANOVA showed that there was a significant interaction of time and target on BMI ($F[1.552, 152.052] = 4.401, p = 0.02$). Post hoc testing of simple effects revealed that there was no statistically significant difference in preoperative BMI between subjects who received STN DBS or GPi DBS ($p = 0.15$). However, at 6 months, the BMI of STN DBS patients was greater than that of GPi DBS patients (mean 2.603 [1.127] kg/m², $p = 0.02$); at 12 months, the difference was also significant (mean 2.361 [1.112] kg/m², $p = 0.04$).

In comparing the effects of DBS therapy on men and women with PD, we found that women had experienced a significant weight gain at the 6-month follow-up (mean 2.89 [0.970] kg, $p = 0.04$) and the 12-month follow-up (3.82 [0.884] kg, $p = 0.001$). Conversely, men with PD who had undergone DBS surgery gained more weight on average by the 3-month follow-up (mean [SE] 3.00 [0.535], $p < 0.001$), the 6-month follow-up (3.97 [0.567], $p < 0.001$),

TABLE 1. Weight gain in PD patients at various follow-up times after placement of a DBS device

Patients w/ PD	Mean Weight Gain (kg)	SE	p Value
All			
3 mos	2.66	0.428	<0.001
6 mos	3.64	0.492	<0.001
12 mos	4.18	0.540	<0.001
Men			
3 mos	3.00	0.535	<0.001
6 mos	3.97	0.567	<0.001
12 mos	4.34	0.676	<0.001
Women			
3 mos	1.86	0.684	0.07
6 mos	2.89	0.970	0.04
12 mos	3.82	0.884	0.001
STN subgroup			
All			
3 mos	2.95	0.552	<0.001
6 mos	4.49	0.588	<0.001
12 mos	4.96	0.678	<0.001
Men			
3 mos	3.18	0.686	<0.001
6 mos	4.60	0.713	<0.001
12 mos	5.14	0.867	<0.001
Women			
3 mos	2.37	0.899	0.10
6 mos	4.19	1.051	0.005
12 mos	4.52	0.985	0.001
GPi subgroup			
All			
3 mos	2.07	0.654	0.02
6 mos	1.93	0.830	0.16
12 mos	2.61	0.833	0.02
Men			
3 mos	2.61	0.825	0.03
6 mos	2.57	0.866	0.04
12 mos	2.61	0.943	0.07
Women			
3 mos	0.98	1.033	>0.999
6 mos	0.65	1.792	>0.999
12 mos	2.60	1.71	0.960

Boldface type indicates statistical significance ($p < 0.05$).

and the 12-month follow-up (4.34 [0.676], $p < 0.001$). Running a mixed-factorial ANOVA to determine the significant difference in weight gain between men and women revealed no significant effect of time and sex on weight gain during the postoperative period ($F[1.79, 175.54] = 0.414, p = 0.64$). Therefore, in our model, sex did not have an impact on weight gain. Furthermore, stratifying weight gain in women and men revealed that, although men in the GPi cohort did have a significant postoperative weight gain by 3 months (mean 2.61 [0.825] kg, $p = 0.03$) and 6

TABLE 2. Increase in BMI in PD patients by target (STN and GPi) after placement of a DBS device

Patients w/ PD	Mean BMI Increase (kg/m ²)	SE	p Value
All			
6 mos	1.35	0.183	<0.001
12 mos	1.54	0.197	<0.001
STN subgroup			
6 mos	1.68	0.226	<0.001
12 mos	1.79	0.262	<0.001
GPi subgroup			
6 mos	0.68	0.283	0.07
12 mos	1.03	0.254	<0.001

Boldface type indicates statistical significance ($p < 0.05$).

months (2.57 [0.866] kg, $p = 0.04$), women in the GPi cohort had no significant weight gain at any of the time intervals. For the STN target, men had a greater mean weight gain than women at 3 months (3.18 [0.686] kg, $p < 0.001$ vs 2.37 [0.899] kg, $p = 0.10$), 6 months (4.60 [0.713] kg, $p < 0.001$ vs 4.19 [1.051] kg, $p = 0.005$), and 12 months (5.14 [0.867] kg, $p < 0.001$ vs 4.52 [0.985] kg, $p = 0.001$).

When comparing LED reduction across time points between targets in PD, a mixed-factorial ANOVA revealed that there was a significant effect of time and target on LED reduction ($F[1.360, 133.235] = 6.339$, $p = 0.007$). Post hoc testing of simple effects revealed that there was no significant difference in preoperative LED between patients who were about to receive STN DBS versus those about to receive GPi DBS ($p = 0.75$). However, at 6 months postoperatively, patients with GPi DBS had a significantly greater LED requirement (mean 229.981 [104.136] LED, $p = 0.03$) than patients with STN DBS. At 12 months postoperatively, the GPi DBS LED requirement (233.307 [102.590] LED, $p = 0.03$) was also significantly greater than for STN DBS. Additionally, for patients with PD, we used Pearson's correlation analysis to evaluate whether a change in LED at 6 and 12 months after surgery was correlated with the weight change that each patient experienced. At the 6-month follow-up, the correlation (r) between change in LED and change in weight was -0.33 ($p < 0.001$). At the 12-month follow-up, the correlation between change in LED and change in weight was -0.41 ($p < 0.001$). These findings suggest that patients with the greatest postoperative reduction in LED may experience the most weight gain.

A multivariate regression analysis was performed on the PD cohort to determine the effect of each variable tested—that is, DBS target, preprocedural BMI, sex, and age—on weight change at 3, 6, and 12 months after DBS device placement as compared with weight before the procedure. At 6 and 12 months postoperatively, reduction in LED was added as a variable to our model (Table 3). The only significant findings from our model were that a lower preprocedural BMI was associated with greater weight gain at 12 months (-0.217 kg per baseline BMI, $p = 0.05$) and that a reduction in LED at 6 and 12 months was negatively correlated with weight gain at those two

intervals (-0.006 kg per unit of LED reduced, $p < 0.001$, and -0.004 kg per unit of LED reduced, $p < 0.001$). These results suggests that patients with greater LED reduction following DBS placement may experience greater weight gain.

Effect of UDPRS Score on Weight Change

The UPDRS score was recorded preoperatively and postoperatively for PD patients. Because of inconsistencies in UPDRS score recording, scores were attained for 70 PD patients; 39 received STN DBS, and 31 received GPi DBS. The mean (SD) preoperative score was 26.43 (10.23), and the mean postoperative score was 20.69 (11.36). The average score decreased by 19.7% (39.2%) compared with the preoperative score ($p < 0.001$). Pearson's correlation analysis revealed that a decrease in the UPDRS score was negatively correlated with weight gain at 12 months ($r = -0.224$), meaning that the greater the postoperative decrease in the UPDRS score, the greater the increase in weight at 12 months. However, that result did not reach statistical significance ($p = 0.06$).

Essential Tremor

The ET cohort consisted of 17 men and 19 women. In general, patients with ET experienced no significant weight gain after DBS device placement; these patients showed a mean (SE) weight gain of 0.69 (0.834) kg at the 3-month follow-up ($p > 0.99$), 0.87 (0.875) kg at the 6-month follow-up ($p > 0.99$), and 0.43 (0.679) kg at the 12-month follow-up ($p > 0.99$). No differences were seen between preoperative and postoperative weights when this cohort was subcategorized on the basis of sex (Table 4). Again, there was a broad range of weight change for both male and female ET patients at 3, 6, and 12 months postoperatively.

Discussion

Weight gain after DBS surgery has been previously described, but because of relatively underpowered studies and wide interindividual variability in reported weight gain, further study is warranted. Additional data will not only benefit patients but also guide treatment and empower future meta-analysis. Furthermore, information regarding lead placement may be instructive as DBS is examined as therapy for obesity.¹⁰

Two separate hypotheses have been proposed as the mechanism of action for weight gain following DBS for PD. The first is the “peripheral” hypothesis in which a reduction in motor symptoms, including dyskinesias and tremor, results in a decrease in energy expenditure and increase in appetite as patients wean from antiparkinsonian medications known to cause nausea and anorexia. The second is an intrinsic “central” hypothesis in which indirect stimulation of the hypothalamus disrupts the normal orexigenic/anorexigenic signals that coordinate food intake.³ Emerging data appear to support a hypothesis that weight gain from GPi DBS mainly results from the peripheral extinguishing of dyskinesias, whereas STN DBS may exhibit both the central and peripheral pathways.

Early studies provided background on the weight phe-

TABLE 3. Demographic and clinical factors associated with weight change among patients with PD

Parameter	Regression Coefficient, β (95% CI)	p Value
3 mos		
Target (STN vs GPi)	-1.38 (-3.688 to 0.928)	0.24
Baseline BMI	-0.148 (-0.365 to 0.070)	0.18
Sex (male vs female)	-2.153 (-4.539 to 0.232)	0.08
Age (per yr)	0.023 (-0.108 to 0.153)	0.73
Reduction in LED (per unit reduced)	NA	
6 mos		
Target (STN vs GPi)	-0.618 (-2.917 to 1.682)	0.60
Baseline BMI	-0.120 (-0.328 to 0.088)	0.25
Sex (male vs female)	-1.167 (-3.455 to 1.121)	0.31
Age (per yr)	0.069 (-0.057 to 0.195)	0.28
Reduction in LED (per unit reduced)	-0.006 (-0.008 to 0.003)	<0.001
12 mos		
Target (STN vs GPi)	0.838 (-1.545 to 3.221)	0.49
Baseline BMI	-0.217 (-0.433 to 0.000)	0.05
Sex (male vs female)	-0.234 (-2.632 to 2.164)	0.85
Age (per yr)	-0.017 (-0.150 to 0.116)	0.80
Reduction in LED (per unit reduced)	-0.004 (-0.006 to -0.002)	<0.001

NA = not applicable.

Weight gain in kilograms at 3, 6, and 12 months after placement of DBS device based on the quantile regression analysis. Boldface type indicates statistical significance ($p < 0.05$).

nomena after DBS and documented both weight gain and energy expenditures. In the study by Montaurier et al.,⁴ 24 patients with PD, on average, gained weight after bilateral STN lead placement at 3 months postprocedure but with high interindividual variability (range -1.5 to 7.9 kg in men and 0.3–5.2 kg in women). Additionally, weight gain differed between men and women; on average, men gained 3.4 kg, and women gained 2.6 kg. Both men and women had their daily energy expenditure reduced after surgery, as measured by physiological testing in calorimetric chambers. Montaurier et al. noted that postoperative daily energy intake was not altered and that the reduction in energy expenditure in the form of improved motor control and the disappearance of levodopa-induced dyskinesias (LIDs) were indicative of future weight gain.

Our PD patient cohort with STN DBS, on average, had gained weight by the 3-month follow-up appointment, and the men in this subgroup had gained more weight on average than the women (3.18 kg in men vs 2.37 kg in women). These results are similar to the findings reported by Montaurier et al.⁴ We saw that the weight gain continued by the 6- and 12-month follow-ups for both sexes (men 4.60 and 5.14 kg vs women 4.19 and 4.52 kg, respectively). Patients with STN DBS were able to reduce their LEDs (-22.7% $\pm$ 31.3% at 6 months in our study, similar to findings reported by Montaurier et al. at 3 months, -40.1% $\pm$ 7.8%), which may have been instrumental in improving nausea or anorexia.

Although, on average, men experienced greater weight gain than women, the difference between the two groups was not statistically significant. Furthermore, women in the GPi group did not have a statistically significant weight

gain at any of the time points. However, as only 11 of our 100 PD patients were women with GPi DBS device placement, these findings could be attributable to an underpowered arm of the cohort. When comparing men and women with GPi DBS to each other, we also found no statistically significant difference between the two groups ($p = 0.25$ at 3 months, $p = 0.28$ at 6 months, and $p > 0.99$ at 12 months), even though male GPi patients did have a statistically significant difference in weight gain when looking only at that cohort.

Our results also contrast with the findings of Montaurier et al.,⁴ who found that there was a significant differ-

TABLE 4. Weight gain among ET patients after placement of a DBS device

Patients w/ ET	Mean Weight Gain (kg)	SE	p Value
All			
3 mos	0.69	0.834	>0.99
6 mos	0.87	0.875	>0.99
12 mos	0.43	0.679	>0.99
Men			
3 mos	0.00	0.796	>0.99
6 mos	0.05	0.906	>0.99
12 mos	-0.17	0.774	>0.99
Women			
3 mos	1.31	1.42	>0.99
6 mos	1.61	1.45	>0.99
12 mos	0.96	1.09	>0.99

ence in the body weight increase in men compared with that in women 3 months after STN DBS (mean [SE] 3.4 [0.6] kg vs 2.6 [0.8] kg). In that study, the authors noted that differences in energy metabolism between the sexes could explain their findings. They noted that men with long-term levodopa treatment had higher than expected basal metabolic rates before surgery, which were then normalized following surgery. However, in women, the basal metabolic rate actually increased following surgery. Montaurier et al.⁴ postulated that these results of increased preoperative basal metabolic rate could be attributed to increased rigidity and possibly LIDs that are then normalized following DBS therapy. In addition, they also found that, although men primarily gained fat-free mass, women mostly gained fat.⁴ Although we noted that weight gain was statistically significant in all PD patients with STN DBS therapy in our study, we found no statistical difference in weight gain between male and female patients treated with STN DBS, which suggests that the target (STN) may play a larger role than sex in weight change following DBS therapy.

Compared with the STN target, the GPi DBS target has been demonstrated to cause less overall weight gain.⁵ We affirm this finding on the basis of our study results. Sauleau et al.⁵ found that, at 6 months, the mean weight gain for 14 GPi DBS patients was 1.7 kg, whereas the mean weight gain for 32 STN DBS patients was 5.7 kg.⁵ Our results demonstrated a mean weight gain of 4.49 kg in STN DBS patients and 1.93 kg in GPi DBS patients. Similarly, Mills et al.² reported that 30 patients with bilateral GPi DBS experienced mild weight loss as opposed to the weight gain seen in 31 patients with bilateral STN DBS. They mentioned that a difference was present in BMI changes at 1 year (STN DBS 0.39% BMI increase vs GPi DBS -0.14% BMI decrease) but that it failed to reach statistical significance. Additionally, they reported percentages of patients with > 10-kg weight gain, similar to those reported by Sauleau et al.²

Locke et al.¹ used data from the 52 patients in the COM-PARE trial (Effect of Deep Brain Stimulation on Motor, Mood, and Cognitive Symptoms in Parkinson's Disease) PD DBS cohort to determine whether there was a difference in weight gain at 6 months after surgery for those implanted with a unilateral lead targeted to either the STN or GPi. Despite documenting weight gain at 6 months postprocedure for all patients (2.2 kg), Locke et al. did not document, as they initially hypothesized, a significant difference in weight gain between their STN (1.95 ± 3.08 kg) and GPi (2.44 ± 4.69 kg) cohorts.¹

In our study, we found a greater weight gain at 6 months among the patients with DBS targeted to the STN (mean 4.49 [0.588] kg) than in those with DBS targeted to the GPi (1.93 [0.830] kg). A factor responsible for this greater weight gain among the STN DBS patients is the implantation of bilateral leads into the STN, which may have led to a bilateral, and therefore more precipitous, reduction in LIDs and energy expenditure. Possible confirmation of this hypothesis is the consistency of the weight gain shown in our study along with that of the Montaurier STN patients at 3 months and the relative discrepancy between our results and those of the Locke STN patients at 6 months.^{1,4}

Locke et al.¹ examined the central hypothesis of STN leads, asserting that there may be current stimulating the

orexigenic/anorexigenic pathways. They attempted to quantify this by assessing binge eating and carbohydrate craving, but this portion of the study was relatively underpowered, given its low participation. No changes in food consumption behaviors were significant.

Despite these findings, other studies have hinted at a central pathway. Novakova et al.⁶ tested food-related hormone levels (leptin, adiponectin, resistin, ghrelin, cortisol, insulin, and thyroid-stimulating hormone) in 27 patients after STN DBS and found only a decrease in overall cortisol levels that persisted at 12 months. Markaki et al.³ documented statistically significant elevations in neuropeptide Y levels at 3 months and ghrelin levels at 6 months after the procedure. Sauleau et al.¹¹ used positron emission tomography to demonstrate that STN DBS and weight gain correlated with metabolic changes in the distributed ventral associative-limbic network in the orbitofrontal, cingulate, and temporal cortices of the brain. These areas are associated with integrating cognitive and affective representations of food and initiating behavioral responses necessary to acquire it.

In our study, LED was recorded preoperatively and at 6 and 12 months postoperatively. Overall, patients required a lower LED postoperatively. Stratifying this finding by target, we concluded that there was a significant difference in the reduction of LED between the STN and GPi cohorts at 6 months (351.896 ± 496.380 units vs 78.030 ± 354.693 units, respectively, $p = 0.006$) and at 12 months (347.433 ± 551.712 units vs 70.242 ± 421.002 units, $p = 0.01$). Several studies have reported similar findings. A meta-analysis conducted by Liu et al.,⁷ which included five other independent studies, revealed that the mean difference in postoperative LED between STN and GPi patients was -320.55 (95% CI -401.36 to -239.73 , $p < 0.001$). These results further promote the hypothesis suggested in a study by Krause et al.⁸ that, although STN stimulation works by directly affecting parkinsonian symptoms, leading to lower LED requirements and hence a decrease in LIDs, GPi stimulation works mainly by reducing the adverse effects of a dopamine agonist, leading to increased drug tolerance.

In our study, patients experienced significant weight gain after DBS for PD but not after DBS for ET (Tables 1 and 4). This result was similar to the findings of Strowd et al.,⁹ who found that, while their PD cohort of patients gained a statistically significant amount of weight following DBS therapy, the ET cohort did not demonstrate a statistically significant increase ($p = 0.38$). That study also found that, when PD patients had DBS VIM implantation, there was significant weight gain (4.1 kg, $p = 0.04$). In our study, only ET patients received VIM-targeted DBS. This finding provides further support for the peripheral hypothesis. Montaurier et al.⁴ postulated the idea that muscle rigidity in PD patients could lead to an increase in energy expenditure, which could contribute to the weight loss that many patients with PD experience. Because DBS therapy leads to a reduction in rigidity, that weight loss could then be normalized following surgery.

Conclusions

The effect of DBS in reducing hyperkinetic symptoms such as tremors and dyskinesias causes weight gain in PD

patients but not ET patients. Without behavioral changes in caloric intake, weight gain can occur after DBS surgery. Increased awareness of this observation can aid in preoperative and postoperative patient counseling. When evaluating patients with PD for DBS implantation, a low BMI may be a consideration. Additionally, those patients with the greatest decrease in LED following DBS implantation could be those most at risk for weight gain. Because of the low patient enrollment at individual institutions, a multicenter study or meta-analysis may be necessary to appropriately power and validate the significance of our findings.

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Disclosures

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Author Contributions

Conception and design: Ponce, Monteferrante, Wilhelmi. Acquisition of data: Monteferrante, Lambert. Analysis and interpretation of data: Ponce, Monteferrante, Wilhelmi. Drafting the article: Ponce, Monteferrante, Wilhelmi. Critically revising the article: Ponce, Monteferrante, Wilhelmi. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Ponce. Statistical analysis: Monteferrante, Wilhelmi. Administrative/technical/material support: Ponce. Study supervision: Ponce, Monteferrante, Wilhelmi.

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