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Short communication

Different psychological and quality-of-life outcomes after subthalamic nucleus deep brain stimulation in Parkinson's disease patients: a prospective study

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ABSTRACT

Background: The present study aimed to evaluate changes in hopelessness, psychological well-being, and quality of life following subthalamic nucleus deep brain stimulation (STN-DBS) in patients with Parkinson's disease (PD). In addition, a secondary exploratory aim was to assess the role of anxiety and depression as predictors of psychological and quality-of-life outcomes after STN-DBS.

Methods: This prospective pre-post study enrolled 70 patients with PD, of whom 64 underwent STN-DBS and were analyzed. The Beck Hopelessness Scale, Ryff's Psychological Well-Being Scale, Short Form-36 Health Survey, and motor (UPDRS-III) and medication-related (LEDD) data were assessed 30 days before STN-DBS (T0) and one year after STN-DBS (T1). In addition, the Beck Depression Inventory-II and State-Trait Anxiety Inventory-Form Y were administered at T0.

Results: After STN-DBS, hopelessness increased in the feelings about the future subscale, and psychological well-being decreased in the autonomy and personal growth subscales. In contrast, quality of life improved in the physical and mental components and in the physical role, general health, and vitality subscales. Moreover, UPDRS-III and LEDD scores decreased. Changes in LEDD showed a concurrent association with the quality-of-life vitality subscale after STN-DBS, while anxiety and depression did not emerge as significant predictors.

Conclusions: The findings suggest that although several quality-of-life dimensions in PD patients improve after STN-DBS, hopelessness related to future feelings and psychological well-being related to autonomy and personal growth worsen. A multidisciplinary approach that integrates neurological and psychological dimensions is essential for identifying, monitoring, and supporting patients who experience adverse psychological changes following STN-DBS.

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1. Introduction

Parkinson's disease (PD) is a chronic and progressive neurodegenerative disorder characterized by neuronal loss and reduced dopamine availability in the nigrostriatal pathways, impairing motor control and several brain systems [1]. In addition to motor symptoms, PD patients often exhibit non-motor symptoms, including sleep and cognitive problems, autonomic dysfunction, and mood and anxiety symptoms, with a significant impact on quality of life (QoL) [2].

Deep brain stimulation (DBS) has emerged as one of the most effective interventions for patients with advanced PD [3]. The efficacy of DBS for motor symptoms and medication outcomes is well established, with several studies demonstrating improvements in bradykinesia, rigidity, tremor, levodopa-induced dyskinesias, and dopaminergic medication requirements [3]. However, DBS could involve several risks, including cognitive side effects and psychological consequences [4]. In this regard, while some research reported improvements in depressive and anxiety symptoms after DBS, others highlighted worsening of affective regulation and psychological well-being, as well as an increased risk of suicidal behavior in specific subgroups of patients after DBS [4–7]. In contrast, the literature provides more consistent evidence of improved QoL after DBS, particularly in the physical and functional domains, following reductions in motor symptoms and increased autonomy in daily activities [8].

Considering these heterogeneous findings, the present study aimed to evaluate changes in hopelessness, psychological well-being, and QoL after subthalamic nucleus (STN) DBS in patients with PD. Moreover, although some studies suggested that anxiety and depression can influence the perception of the functional benefits of DBS and lead to complex psychological adaptation to the disease despite motor improvement, such evidence in the literature remains preliminary [8,9]. Therefore, a secondary exploratory aim of the present study was to assess the role of anxiety and depression as potential predictors of psychological and QoL outcomes following STN-DBS.

2. Methods

2.1. Participants and procedures

This prospective, single-arm, pre-post study was conducted at the Neurology Unit of the Policlinico Universitario A. Gemelli IRCCS, Rome. Participants were recruited by the Lazio DBS Study Group. The inclusion criteria were: (1) diagnosis of idiopathic PD according to the clinical criteria of the Movement Disorder Society; (2) disease duration of four years or longer; (3) presence of clinically significant motor symptoms or dyskinesias limiting daily functioning; (4) age below 75 years; (5) neurosurgical eligibility for DBS, as determined by a multidisciplinary team; (6) adequate comprehension of Italian. The exclusion criteria included: (1) dementia or clinically significant cognitive impairment, as assessed by the neurology unit team as part of the preoperative assessment using a Mini-Mental State Examination cut-off score of < 24; (2) current diagnosis of major psychiatric disorders (e.g., psychotic, mood, anxiety, and substance use disorders).

The study was approved by the Ethics Committee of the Policlinico Universitario A. Gemelli IRCCS-Università Cattolica del Sacro Cuore of Rome (ID protocol: 4578) and was conducted in accordance with the Declaration of Helsinki (1964) and the TREND guidelines (Table S1, Supplementary Material). All participants provided written informed consent. Assessments were performed within 30 days prior to DBS (T0) and 1 year after (T1). At T0, sociodemographic, clinical, and motor (Unified Parkinson's Disease Rating Scale Part III, "UPDRS-III", in ON- and OFF-medication conditions) and medication-related (levodopa equivalent daily dose, "LEDD") data were collected. Regarding motor data assessments, the OFF-medication condition was defined by an overnight 12-h washout of levodopa. The ON-medication condition was reached by administering immediate-release levodopa at 150% of the usual morning levodopa dose, with motor assessment performed approximately 45 min later, when an optimal on-state was reached, according to the physician and patient. Moreover, self-report questionnaires assessing hopelessness, psychological well-being, QoL, trait anxiety, and depression were administered. At T1, motor (UPDRS-III in ON- and OFF-medication conditions) and medication-related (LEDD) data were collected again, and participants were reassessed using the same self-report measures evaluating hopelessness, psychological well-being, and QoL. At T1, motor data assessments were performed with DBS stimulation ON in both the OFF- and ON-medication conditions, using the same criteria as at T0.

2.2. Deep brain stimulation surgery

Experienced functional neurosurgeons performed bilateral DBS. Leads were placed in the STN ($n = 64$), internal globus pallidus (GPi; $n = 4$), and ventral intermediate nucleus (VIM; $n = 2$), using an intraoperative O-arm-controlled frameless and fiducial-less Nexframe system with StealthStation S8 navigation. To reduce heterogeneity related to the DBS target, the cohort of participants analyzed in the present study was limited to those who underwent STN-DBS. The sensorimotor region of the target nucleus was identified using single-track, multipass microelectrode recordings, and intraoperative microstimulation was used to assess therapeutic and side-effect thresholds. After lead implantation, the implantable pulse generator was placed under general anesthesia. Postoperative computed tomography scans were obtained to rule out hemorrhage and verify lead location. Stimulation was switched on postoperatively with standard initial programming (pulse width 60 μs and frequency 130 Hz), followed by individual adjustments of stimulation parameters and antiparkinsonian medication regimens based on clinical response.

2.3. Measures

The Beck Hopelessness Scale (BHS), a 20-item true/false self-report questionnaire, was used to measure three cognitive-affective dimensions of hopelessness: feelings about the future, loss of motivation, and future expectations. Higher scores indicate greater hopelessness.

Ryff's Psychological Well-Being Scale (PWBS), an 84-item self-report questionnaire rated on a 6-point Likert scale (1 = strongly disagree to 6 = strongly agree), was used to assess six dimensions of psychological well-being: autonomy, mastery of the environment, personal growth, positive relationships with others, purpose in life, and self-acceptance. In addition, the PWBS total score was evaluated by summing the scores across the six dimensions. Higher scores on each dimension and on the total score indicate greater psychological well-being.

The Short Form-36 Health Survey (SF-36), a 36-item self-report questionnaire, was used to evaluate perceived health-related QoL, including eight subscales: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health. Each subscale score ranges from 0 to 100. Furthermore, the Physical Component Summary and Mental Component Summary scores were calculated by summing factor-weighted scores across all eight subscales, according to the standard SF-36 version 1 norm-based scoring algorithm [10]. Specifically, each of the eight subscale scores was standardized using the corresponding mean and standard deviation from the U.S. general population normative sample, multiplied by the respective factor-score coefficient for the Physical Component Summary and Mental Component Summary, and then summed across the eight subscales. The resulting component summary scores were transformed to norm-based *T*-scores with a mean of 50 and a standard deviation of 10. The normative values and factor-score coefficients used for scoring are reported in Table S2 of the Supplementary Material. Higher subscale and summary scores indicate better QoL.

The State-Trait Anxiety Inventory-Form Y (STAI-Y), a 40-item self-report questionnaire rated on a 4-point Likert scale (1 = almost never

to 4 = almost always), was used to assess trait anxiety. Higher scores indicate higher levels of trait anxiety. A score ≥ 44 was considered above the cut-off for clinically relevant trait anxiety levels.

The Beck Depression Inventory-II (BDI-II), a 21-item self-report questionnaire rated on a 4-point Likert scale, was used to assess the severity of depressive symptoms. Higher scores indicate more severe depressive symptoms. A score ≥ 15 was considered above the cut-off for clinically relevant depressive symptoms in patients with PD.

2.4. Statistical analyses

After descriptive analyses, baseline sample characteristics were compared between participants who completed and those who did not complete the T1 assessment, and between participants with complete and incomplete psychological and QoL data. Continuous baseline characteristics were compared using Mann-Whitney U tests, and categorical variables using Fisher's exact test. Paired-samples Student's *t*-tests or Wilcoxon tests for non-normally distributed variables were used to compare T0 and T1 scores on the BHS total and subscales, the PWBS total and subscales, the SF-36 components summary and subscales, as well as the UPDRS-III in ON- and OFF-medication conditions and the LEDD. Results were corrected for multiple comparisons using the Benjamini-Hochberg false discovery rate (FDR) procedure.

An a priori power analysis for paired-samples t-tests indicated that 52 participants were required to detect an effect size of 0.40, with $\alpha = .05$ and 80% power. Recruitment was increased by at least 25% to account for attrition and missing follow-up assessments.

To explore predictors of psychological and QoL outcomes that showed significant pre-post differences following STN-DBS, baseline-adjusted linear regression models were conducted. In each model, outcome scores at T1 that showed significant pre-post differences following STN-DBS were entered as dependent variables, and the corresponding outcome scores at T0 were included as adjustment variables to account for baseline levels. Specifically, two separate sets of regression models were conducted. The primary set examined baseline anxiety and depression as predictors of psychological and QoL outcomes. STAI-T and BDI-II scores at T0 were entered in the models as predictors in addition to the outcome scores at T0. A second exploratory set examined concurrent associations between changes following STN-DBS in motor and medication-related data and psychological and QoL outcomes. Changes in UPDRS-III scores under the OFF-medication condition and in LEDD ($\Delta = T1 - T0$) were entered in the models as predictors in addition to the outcome scores at T0. For both sets of regression models, the enter method was used, with variables of interest entered simultaneously after adjustment for the outcome score at T0. Regarding regression model diagnostics, multicollinearity was evaluated using variance inflation factors (VIFs), and outlying and influential observations were assessed using standardized residuals and Cook's distance. The VIFs (values < 5) did not indicate problematic multicollinearity, and the standardized residuals (absolute values < 3) and Cook's distance (values < 1) did not suggest major outlying or influential cases (Tables S3 and S4, Supplementary Material). The assessment also included inspection of residual-versus-fitted, residual-versus-predictor, and Q-Q plots, which did not indicate substantial departures from linearity, homoscedasticity, or normality of the residuals.

Significance was set at $p < .05$ for all analyses conducted. Missing data were managed using the pairwise deletion method to maximize the use of the available observed data. Accordingly, participants were excluded only from analyses of variables for which data were unavailable, and the size of the analyzed sample could vary across outcomes. To assess the robustness of the results, complete-case sensitivity analyses were conducted. The pre-post STN-DBS comparisons were repeated among participants with complete paired data across all psychological and QoL outcomes ($n = 43$) and among participants with complete paired data across all motor and medication-related outcomes ($n = 42$), using the same statistical tests and correction procedure as in the primary analyses. Statistical analyses were performed using JASP software.

3. Results

The recruited sample comprised 70 patients with PD. Of these, 64 underwent STN-DBS and were included in the analyses. A detailed description of the participant flow from enrollment to the final analytic cohort is shown in Fig. S1 of the Supplementary Material. Of the 64 participants included in the analytic cohort, 58 completed the T1 assessment, although individual questionnaire and clinical measures were not available for all participants at follow-up. As paired analyses required data for the corresponding measure at both T0 and T1, paired sample sizes varied across measures (Table S5, Panel A, Supplementary Material). No significant differences in baseline characteristics were observed between T1 completers and non-completers or between participants with complete and incomplete psychological and QoL measures (Table S5, Panels B and C, Supplementary Material).

Most of the participants were male (40/64; 63%), and the mean age was 58.48 ± 7.27 years. Regarding the clinical phenotype, 44 patients (69%) presented with the akinetic-rigid form, 13 patients (20%) with the tremor-dominant phenotype, and 7 patients (11%) with the mixed type. The mean disease duration was 12.71 ± 7.36 years. The LEDD averaged 1170.00 ± 477.40 mg/day (range 200–2734 mg/day). Motor performance, assessed using the UPDRS-III, yielded a mean score of 38.09 ± 13.89 in the OFF-medication condition and 18.56 ± 7.83 in the ON-medication condition. Regarding baseline data for trait anxiety and depression, the mean STAI-T and BDI-II scores were 39.88 ± 8.62 and 10.28 ± 6.45, respectively. Twenty-four patients (38%) met the clinical cut-off for the STAI-T, and 19 (30%) for the BDI-II.

Differences between pre- and post-STN-DBS assessments in hopelessness, psychological well-being, QoL, and motor and medication-related outcomes are reported in Table 1, Fig. 1, and Fig. S2 of the Supplementary Material. The Feelings about the Future subscale of the BHS showed a significant increase from pre-STN-DBS to post-STN-DBS. Regarding psychological well-being, the PWBS Total Score and the Autonomy and Personal Growth dimensions showed significant decreases from pre-STN-DBS to post-STN-DBS. The result for PWBS Total Score did not remain significant after applying the FDR correction. In contrast, for QoL, significant increases were observed in the SF-36 Physical Component Summary and Mental Component Summary, as well as in the Role Physical, General Health, Vitality, and Social Functioning dimensions from pre-STN-DBS to post-STN-DBS. The result for SF-36 Social Functioning did not remain significant after applying the FDR correction. Lastly, significant decreases were observed in UPDRS-III under both ON- and OFF-medication conditions and in LEDD.

Complete-case sensitivity analyses showed results consistent with the primary analyses, with no changes in the FDR-significant findings for psychological and QoL outcomes or for motor and medication-related outcomes (Table S6, Supplementary Material).

Results of the primary set of baseline-adjusted multiple linear regression analyses showed that baseline trait anxiety and depression did not emerge as significant predictors of post-STN-DBS psychological and QoL outcomes. The overall models were significant for PWBS Autonomy, $F(3, 40) = 8.20$, $p < .001$ (accounting for 38.1% of the variance) and for SF-36 Role Physical, $F(3, 41) = 4.75$, $p = .006$ (accounting for 25.8% of the variance). In both models, higher corresponding baseline outcome scores were associated with higher post-STN-DBS outcome scores (PWBS Autonomy: $B = 0.72$, $SE = 0.15$, $\beta = 0.60$, $p < .001$; SF-36 Role Physical: $B = 0.36$, $SE = 0.12$, $\beta = 0.42$, $p = .005$). No statistically significant overall regression models were found for other outcomes (all $p > .05$; Table S3, Supplementary Material).

Regarding the second exploratory set of baseline-adjusted multiple linear regression analyses, the results showed that changes in LEDD were significantly associated with post-STN-DBS SF-36 Vitality scores. The overall model for SF-36 Vitality was significant, $F(3, 32) = 3.36$,

Table 1
Pre-post STN-DBS differences in hopelessness, psychological well-being, quality of life, and motor and medication-related outcomes.

Variables	Paired *n*	Pre-STN-DBS (mean ± SD)	Post-STN-DBS (mean ± SD)	Test statistic	*p*-value	p_{FDR}	Effect size (95% CI)
Hopelessness							
BHS Total Score	47	6.34 ± 4.30	6.45 ± 4.68	$t(46) = -1.24$	0.221	0.266	$d = -0.18$ (−0.47; 0.11)
BHS Feelings about Future	47	1.50 ± 1.59	2.04 ± 1.84	$Z = -2.36$	0.018	0.043	$r = -0.49$ (−0.73; −0.13)
BHS Loss of Motivation	47	1.70 ± 1.93	1.66 ± 1.81	$Z = -0.63$	0.531	0.554	$r = -0.13$ (−0.49; 0.27)
BHS Future Expectations	47	2.88 ± 2.00	2.34 ± 1.46	$Z = 1.54$	0.119	0.179	$r = 0.30$ (−0.07; 0.60)
Psychological well-being							
PWBS Total Score	44	314.40 ± 36.22	296.6 ± 44.37	$Z = 2.11$	0.036	0.072	$r = 0.38$ (0.05; 0.63)
PWBS Autonomy	44	51.30 ± 8.49	48.53 ± 9.81	$t(43) = 2.95$	0.005	0.018	$d = 0.44$ (0.13; 0.75)
PWBS Environmental Mastery	44	50.77 ± 7.37	48.82 ± 7.63	$Z = 1.84$	0.066	0.114	$r = 0.34$ (−0.01; 0.62)
PWBS Personal Growth	44	56.62 ± 8.16	52.56 ± 12.17	$Z = 2.50$	0.013	0.034	$r = 0.45$ (0.13; 0.69)
PWBS Positive Relations	44	53.07 ± 14.42	48.18 ± 7.55	$Z = 1.40$	0.162	0.217	$r = 0.27$ (−0.09; 0.57)
PWBS Purpose in Life	44	53.25 ± 7.77	50.84 ± 10.08	$Z = 1.29$	0.199	0.251	$r = 0.24$ (−0.12; 0.54)
PWBS Self-Acceptance	44	49.38 ± 7.53	47.71 ± 8.68	$Z = 0.28$	0.787	0.787	$r = 0.05$ (−0.32; 0.41)
Quality of life							
SF-36 PC Summary	45	39.23 ± 6.15	43.29 ± 6.50	$t(44) = -3.37$	0.002	0.008	$d = -0.50$ (−0.81; −0.19)
SF-36 MC Summary	45	33.27 ± 9.42	40.62 ± 12.08	$t(44) = -3.58$	<0.001	0.005	$d = -0.53$ (−0.84; −0.22)
SF-36 Physical Functioning	45	47.28 ± 20.66	55.57 ± 23.09	$t(44) = -1.64$	0.108	0.173	$d = -0.24$ (−0.54; 0.05)
SF-36 Role Physical	45	53.39 ± 21.37	60.00 ± 18.40	$t(44) = -2.37$	0.022	0.049	$d = -0.35$ (−0.65; −0.05)
SF-36 Bodily Pain	45	57.79 ± 16.03	62.43 ± 16.88	$t(44) = -1.47$	0.147	0.208	$d = -0.22$ (−0.51; 0.08)
SF-36 General Health	45	43.87 ± 20.54	56.07 ± 18.21	$t(44) = -2.69$	0.010	0.030	$d = -0.40$ (−0.70; −0.10)
SF-36 Vitality	45	27.36 ± 21.66	67.80 ± 29.75	$Z = -5.23$	<0.001	<0.001	$r = -1.00$ (−1.00; −1.00)
SF-36 Social Functioning	45	24.18 ± 35.35	44.02 ± 42.88	$Z = -2.04$	0.041	0.076	$r = -0.49$ (−0.76; −0.06)
SF-36 Role Emotional	45	47.44 ± 43.32	59.24 ± 40.50	$Z = -0.91$	0.364	0.416	$r = -0.21$ (−0.59; 0.24)
SF-36 Mental Health	45	48.69 ± 13.84	49.50 ± 15.22	$Z = -0.77$	0.445	0.486	$r = -0.16$ (−0.52; 0.24)
Motor and medication-related outcomes							
UPDRS-III ON-medication	44	18.56 ± 7.83	15.83 ± 6.92	$t(43) = 3.23$	0.002	0.010	$d = 0.49$ (0.17; 0.80)
UPDRS-III OFF-medication	45	38.09 ± 13.89	26.96 ± 9.55	$t(44) = 6.45$	<0.001	<0.001	$d = 0.96$ (0.60; 1.31)
LEDD	51	1170.0 ± 477.4	708.8 ± 388.1	$t(50) = 6.58$	<0.001	<0.001	$d = 0.93$ (0.59; 1.25)

Note. STN-DBS = subthalamic nucleus deep brain stimulation; BHS = Beck Hopelessness Scale; PWBS = Ryff's Psychological Well-Being Scale; SF-36 = Short Form-36 Health Survey; PC = Physical Component; MC = Mental Component; UPDRS-III = Unified Parkinson's Disease Rating Scale Part III; LEDD = levodopa equivalent daily dose; *SD* = standard deviation; FDR = false-discovery rate correction; *CI* = confidence interval; *t* = Student's *t*-test; *Z* = Wilcoxon test; *d* = Cohen's *d*; *r* = rank-biserial correlation. Effect sizes were calculated using the T0–T1 difference, for which negative values indicate higher scores at T1, whereas positive values indicate lower scores at T1.

$p = .031$, accounting for 23.9% of the variance. Smaller reductions in LEDD were associated with lower post-STN-DBS SF-36 Vitality scores ($B = -0.03$, $SE = 0.009$, $\beta = -0.43$, $p = .011$). The overall model for PWBS Autonomy was also significant, $F(3, 31) = 7.86$, $p < .001$, accounting for 43.2% of the variance. Higher corresponding baseline outcome scores were associated with higher post-STN-DBS outcome scores ($B = 0.78$, $SE = 0.17$, $\beta = 0.65$, $p < .001$). No statistically significant overall regression models were found for other outcomes (all $p > .05$). Across the models examined, changes in UPDRS-III under the OFF-medication condition were not significantly associated with psychological and QoL outcomes (Table S4, Supplementary Material).

4. Discussion

The present study examined changes in hopelessness, psychological well-being, and QoL after STN-DBS in patients with PD and the role of trait anxiety and depression as potential predictors of these outcomes. The main results showed that after STN-DBS, hopelessness related to future feelings and psychological well-being related to autonomy and personal growth worsened, while QoL improved in several domains. These changes occurred in the context of significant reductions in UPDRS-III scores in both ON- and OFF-medication conditions and in LEDD after STN-DBS.

The increase in hopelessness related to feelings about the future, together with the decrease in psychological well-being related to autonomy and personal growth, suggests that improvements in some clinical domains following STN-DBS may coexist with challenges in psychological adaptation. This result is consistent with previous studies showing heterogeneous psychological trajectories after DBS and reinforces the importance of systematically monitoring suicidality-related constructs during intervention follow-up [4–7]. In this regard, while surgery can lead to rapid improvement in motor functioning, as highlighted by the present study's findings, some patients may not concurrently experience the same positive outcomes at the psychological level [11]. One possible interpretation is that psychological adaptation to changes in functional status, daily roles, or personal expectations might contribute to this divergence in outcomes. However, these processes were not directly assessed in the present study. Therefore, further research is needed to better understand the factors underlying the observed psychological changes.

In contrast, alongside improvements in motor and medication-related outcomes, several QoL domains increased after STN-DBS, including physical and mental components, role physical, general health, and vitality. These findings are in line with previous studies showing that DBS reduces motor complications and enhances physical well-being and QoL [8,12]. The observed improvement in vitality could be clinically relevant, as it reflects a subjective increase in energy and motivation that may encourage greater participation in daily activities and social interaction. Likewise, improvements in role physical and general health further suggest that patients may perceive fewer physical health limitations and a more favorable overall health status following STN-DBS. Overall, these findings suggest improvements following STN-DBS not only for motor and medication-related outcomes but also for broader aspects of patient well-being and QoL [5,8].

Moreover, the results of the exploratory regression analyses showed that changes in LEDD were significantly associated with the QoL vitality domain after STN-DBS. Smaller reductions in LEDD were associated with lower QoL vitality scores. In contrast, baseline trait anxiety and depression, as well as changes in UPDRS-III under the OFF-medication condition, were not significantly associated with psychological and

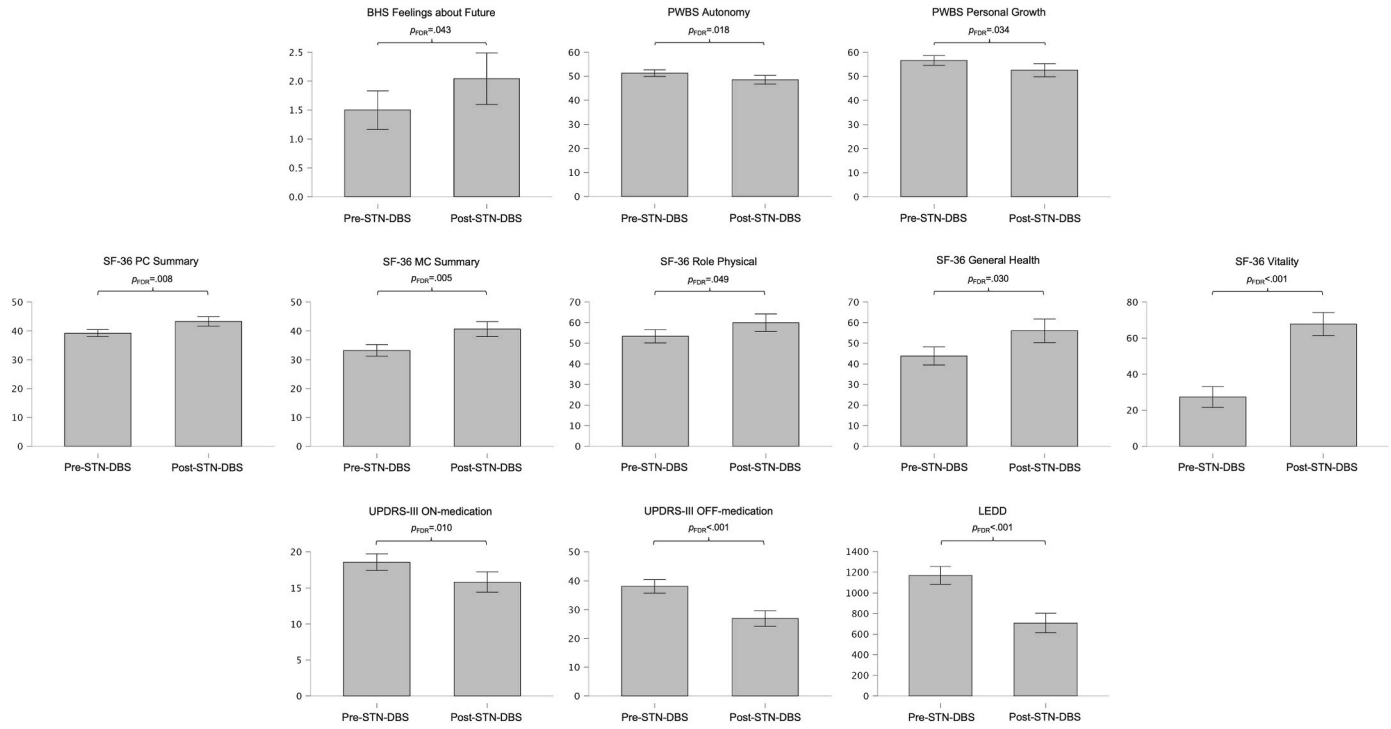

Fig. 1. Bar plots of significant pre-post STN-DBS differences in hopelessness, psychological well-being, quality of life, and motor and medication-related outcomes. *Note*. Bars represent means, and error bars indicate 95% CIs. STN-DBS = subthalamic nucleus deep brain stimulation; FDR = false-discovery rate correction; BHS = Beck Hopelessness Scale; PWBS = Ryff's Psychological Well-Being Scale; SF-36 = Short Form-36 Health Survey; PC = physical component; MC = mental component; UPDRS-III = Unified Parkinson's Disease Rating Scale Part III; LEDD = levodopa equivalent daily dose.

QoL outcomes. Although these findings did not support the results of previous studies showing that anxiety and depression were associated with DBS outcomes [8,9], they are consistent with other research reporting that changes in LEDD would contribute to postoperative QoL outcomes following DBS in PD [13]. Clinically, the results of the present study support the relevance of careful monitoring of medication changes when evaluating postoperative functioning to identify patients who may benefit from more individualized rehabilitative support after STN-DBS. However, these findings should be interpreted with caution, given the limited sample size included in the analyses and the number of regression models examined.

Despite the relevant findings, several limitations must be considered. The absence of a control group that did not undergo STN-DBS and was matched for disease duration and other relevant clinical factors represents a significant limitation of the present study, as it precludes attributing the observed changes specifically to STN-DBS or distinguishing them from changes related to PD progression or other time-dependent clinical factors. Therefore, the results should be interpreted with caution as changes following STN-DBS rather than as treatment effects. Future studies should adopt controlled designs that include a control group of matched PD patients not undergoing STN-DBS. Such study designs would allow for a more accurate distinction between STN-DBS-related changes, treatment-related factors, and the natural course of PD. In addition, the dropout rate may have introduced selection bias, potentially reducing the sample's representativeness. Although recruitment was increased to account for attrition and missing follow-up assessments, the achieved paired-sample sizes ranged from 44 to 51 across examined outcomes and were below the prespecified target of 52 participants, potentially reducing statistical power. It should also be considered that the reasons for missing questionnaires or clinical data were not systematically recorded. Therefore, it is not feasible to determine with certainty the mechanism underlying the missing data, nor can potential bias related to these data be ruled out. Moreover, the one-year follow-up does not allow evaluation of longer-term outcome trajectories. Future research should include longer follow-up assessments to clarify the trajectories of psychological and QoL outcomes over time after STN-DBS. It should also be noted that although limiting the analytic cohort to patients undergoing STN-DBS reduced heterogeneity related to the stimulation target, the present findings may not be generalizable to patients undergoing DBS at other targets. Therefore, further studies, including adequately powered cohorts across different DBS targets, are needed to investigate whether postoperative psychological and QoL outcomes differ by stimulation target. Another limitation concerns the lack of data regarding postoperative dyskinesia. In this regard, given the potential relationship among dyskinesia, medication changes, and psychological outcomes, the absence of such data limited the interpretation of the study's results. Finally, the exploratory regression models explained only a modest-to-moderate proportion of variance (23.9%–43.2%), suggesting that a substantial proportion of individual variability remains unexplained and that other psychological, clinical, and surgical factors may contribute to postoperative psychological and QoL outcomes. The relatively small analytic samples ($n = 35$–47), along with the multiple regression models examined, may also limit the robustness of the estimated associations and increase their susceptibility to sample-specific findings. Future studies with larger sample sizes should include a broader range of predictors to better identify factors associated with postoperative outcomes and to support personalized care.

5. Conclusion

The findings of the present study suggest improvements in several dimensions of QoL, as well as in motor and medication-related outcomes, among patients with advanced PD following STN-DBS. At the same time, these improvements may coexist with worsening in specific psychological domains, including hopelessness about the future, autonomy, and personal growth. Moreover, changes in LEDD showed a concurrent association with the postoperative QoL vitality domain, while anxiety and depression did not emerge as significant predictors.

These results support a multidisciplinary STN-DBS care pathway that integrates neurological, psychiatric, psychological, and rehabilitative expertise. Assessment of postoperative medication changes may help plan targeted supportive interventions to support adjustment after STN-DBS. Postoperative follow-up should also include monitoring of hopelessness related to future feelings and specific psychological well-being dimensions, including autonomy and personal growth. Overall, a bio-psychosocial approach may facilitate the identification and monitoring of potential psychological risks following STN-DBS and support individualized care for patients with PD.

CRediT authorship contribution statement

Marianna Mazza: Writing – review & editing, Supervision, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Giuseppe Marano:** Conceptualization, Data curation, Formal analysis, Methodology, Project administration, Writing – review & editing. **Giorgio Veneziani:** Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization. **Francesco Maria Lisci:** Writing – original draft, Investigation, Data curation, Conceptualization. **Emanuele Giraldi:** Writing – original draft, Visualization, Formal analysis, Data curation, Conceptualization. **Isabella Imbimbo:** Writing – original draft, Project administration, Investigation. **Caterina Brisi:** Writing – original draft, Project administration, Conceptualization. **Elisabetta Benini:** Writing – original draft, Investigation, Data curation. **Emanuela De Chiara:** Writing – original draft, Investigation, Data curation, Conceptualization. **Luca Lo Giudice:** Writing – original draft, Investigation, Conceptualization. **Marco Massetti:** Writing – original draft, Investigation, Data curation. **Francesca Bardi:** Writing – original draft, Investigation, Data curation. **Claudia Calderoni:** Writing – original draft, Investigation, Data curation. **Alessandro Giannico:** Writing – original draft, Investigation, Conceptualization. **Luca Onori:** Writing – original draft, Methodology, Data curation. **Alice Calarco:** Writing – original draft, Data curation. **Francesco Bove:** Writing – original draft, Methodology, Conceptualization. **Carla Piano:** Writing – original draft, Methodology, Conceptualization. **Daniela Pia Rosaria Chieffo:** Writing – original draft, Investigation, Conceptualization. **Carlo Lai:** Writing – review & editing, Writing – original draft, Supervision, Formal analysis. **Paolo Calabresi:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Anna Rita Bentivoglio:** Writing – review & editing, Supervision, Investigation, Data curation, Conceptualization. **Gabriele Sani:** Writing – review & editing, Supervision, Project administration, Investigation, Formal analysis, Data curation, Conceptualization.

Ethics declaration

Written informed consent to take part in the study and to publish the article has been obtained from all participants or their legal representatives. The privacy rights of participants have been observed.

This study was performed in compliance with relevant laws, regulatory frameworks and guidelines where the research took place. This study was approved by the Ethics Committee of the Policlinico Universitario A. Gemelli IRCCS-Università Cattolica del Sacro Cuore of Rome. (Approval No. 4578)

Data availability statement

The data are available upon reasonable request from the corresponding author.

Ethics statement

This study was approved by the Ethics Committee of the Policlinico Universitario A. Gemelli IRCCS-Università Cattolica del Sacro Cuore of Rome (ID protocol: 4578). All participants provided their written informed consent prior to participation in the study.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Francesco Bove reports a relationship with Boston Scientific Corporation that includes: consulting or advisory. Carla Piano reports a relationship with Boston Scientific Corporation that includes: consulting or advisory. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2026.108972.

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