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Long-term effects of subthalamic nucleus deep brain stimulation on speech in Parkinson's disease

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Bilateral subthalamic nucleus deep brain stimulation (STN-DBS) is an effective treatment in advanced Parkinson's Disease (PD). However, the effects of STN-DBS on speech are still debated, particularly in the long-term follow-up. The objective of this study was to evaluate the long-term effects of bilateral STN-DBS on speech in a cohort of advanced PD patients treated with bilateral STN-DBS. Each patient was assessed before surgery through a neurological evaluation and a perceptual-acoustic analysis of speech and re-assessed in the long-term in different stimulation and drug conditions. The primary outcome was the percentage change of speech intelligibility obtained by comparing the postoperative on-stimulation/off-medication condition with the preoperative off-medication condition. Twenty-five PD patients treated with bilateral STN-DBS with a 5-year follow-up were included. In the long-term, speech intelligibility stayed at the same level as preoperative values when compared with preoperative values. STN-DBS induced a significant acute improvement of speech intelligibility (p < 0.005) in the postoperative assessment when compared to the on-stimulation/off-medication and off-stimulation/off-medication conditions. These results highlight that STN-DBS may handle speech intelligibility even in the long-term.

Bilateral subthalamic nucleus deep brain stimulation (STN-DBS) represents a short and long-term effective treatment in advanced Parkinson's Disease (PD)^{1,2}. However, the long-term effects of bilateral STN-DBS on axial features^{3,4} and different speech variables are still debated. After surgery, PD patients may develop heterogeneous profiles of dysarthria related to the possible spreading of current to cerebellothalamic, cortico-bulbar, cortico-spinal and pallido-fugal levels^{5,6}. Moreover, it has been previously reported that speech intelligibility may worsen 1 year after surgery when compared with those under a control group under optimal medical treatment⁷. The majority of the studies regarding the effects of STN-DBS on speech focused on short-term follow-up⁷⁻¹¹ while few studies have assessed the long-term effects^{2,12-14}. In particular, a previous study reported a worsening of speech intelligibility at five and eight years after surgery in the off-medication condition¹², while another acoustic study reported variation of the long-term after surgery¹⁴. The objective of this study was to evaluate

¹Neurology Unit, Department of Neuroscience, S. Agostino Estense Hospital, Azienda Ospedaliero-Universitaria di Modena, Modena, Italy. ²Neurology Unit, Neuromotor & Rehabilitation Department, Azienda USL-IRCCS di Reggio Emilia, Viale Risorgimento 80, 42123 Reggio Emilia, Italy. ³Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena, Italy. ⁴LAM – Motion Analysis Laboratory, Neuromotor and Rehabilitation Department, San Sebastiano Hospital, Azienda USL-IRCCS di Reggio Emilia, Correggio (Reggio Emilia), Italy. ⁵Division of Neuroradiology, Department of Neuroscience, Nuovo Ospedale Civile S. Agostino Estense, Modena, Italy. ⁶Department of Neurology and Stroke Center, IRCCS Istituto Delle Scienze Neurologiche di Bologna, Maggiore Hospital, Bologna, Italy. ⁷Department of Clinical and Movement Neurosciences, UCL Queen Square Institute of Neurology, London, UK. ⁸Nuclear Medicine Unit, Azienda Unità Sanitaria Locale-IRCCS di Reggio Emilia, Reggio Emilia, Italy. ¹⁰Grenoble Alpes University, Division of Neurology, Centre Hospitalier Universitaire de Grenoble, Grenoble Institute of Neuroscience, Grenoble, France. ¹¹Aix-Marseille Univ, CRNS, LPL, Aix-en-Provence, France. ¹²These authors contributed equally: Annalisa Gessani and Francesco Cavallieri. [⊠]email: Francesco.Cavallieri@ausl.re.it the long-term (five years) effects of bilateral STN-DBS on speech in advanced PD patients using a standardized perceptual-acoustic analysis of speech. In the following paragraphs we will report the results of the study, followed by the discussion of these findings before finally describing the methodology of the study.

Results

Patient population. From 2012 to 2017, 40 PD patients underwent STN-DBS. Of these, fifteen subjects were excluded from the study because of missing data (eight patients), lack of consent to participate (four patients), and non-native Italian speakers (three patients). The remaining 25 PD patients with a median follow-up of five years after surgery (range 3–7 years) were included (males: 18; disease duration at surgery: 10.44 ± 4.62] years; age at surgery: 58.40 ± 5.73] years; age at PD onset 47.76 ± 5.63] years). Nineteen patients were included in the PIGD subtype, five in the indeterminate, and one in the TD subtype. Genetic assessment revealed heterozygous mutation in the GBA gene in three patients (12%). Preoperative brain-MRI revealed the presence of white matter hyperintensities of vascular origin in four patients (16%). The mean preoperative levodopa responsiveness was $62.24\% (\pm 16.38\%)$. A detailed description of stimulation parameters and settings is reported in Table 1, while the changes of the different speech and clinical variables in the different conditions tested are shown in Table 2. Concerning the perceptual assessment of dysarthria severity, a significant reduction of the score was found in all the three postoperative conditions tested when compared with the preoperative ones. On the contrary, no significant differences were found by comparing the different postoperative conditions with each other.

Primary outcomes. In the long-term and at the group level, speech intelligibility did not significantly worsen with respect to preoperative values when comparing the postoperative on-stimulation/off-medication condition with the preoperative off-medication condition (z = -0.371, p = 0.710). The shutdown of the stimulation led to an acute significant worsening of speech intelligibility in the postoperative assessment (z = -3.500, p < 0.001) when comparing the on-stimulation/off-medication and off-stimulation/off-medication conditions. Furthermore, the assessment of disease progression effects on speech intelligibility obtained when comparing the postoperative off-stimulation/off-medication condition with the preoperative off-medication condition showed a significant worsening with respect to preoperative values (z = -2.92, p < 0.005). Analyzing the long-term postoperative changes of speech intelligibility at the individual level for each patient, sixteen patients were classified as "stable" while the remaining nine patients integrated a "worsened" subgroup (Fig. 1). Compared to

Stimulation parameters and settings	Total <i>n</i> =25 N. (%), mean, [±SD]; median {range}
Frequency setting	
High frequency	18 (72.00%)
Low frequency	7 (28.00%)
Left STN	
Single monopolar stimulation	20 (80.00%)
Bipolar stimulation	1 (4.00%)
Double monopolar stimulation	4 (16.00%)
Contact 0 active as cathode	1 (4.00%)
Contact 1 active as cathode	14 (56.00%)
Contact 2 active as cathode	13 (52.00%)
Contact 3 active as cathode	2 (8.00%)
Voltage (V)	2.704 [±0.731]; 2.800 {0.652-3.900}
Frequency (Hz)	133.600 [±31.73]; 130.000 {70.000-180.000}
Pulse width (us)	64.800 [±11.225]; 60.000 {60.000-90.000}
Power of stimulation	68.230 [±31.042]; 69.680 {4.240-135.871}
Right STN	
Single monopolar stimulation	23 (92.00%)
Bipolar stimulation	0 (0.00%)
Double monopolar stimulation	2 (8.00%)
Contact 0 active as cathode	2 (8.00%)
Contact 1 active as cathode	15 (60.00%)
Contact 2 active as cathode	10 (40.00%)
Contact 3 active as cathode	0 (0.00%)
Voltage (V)	2.521 [±0.775]; 2.700 {0.746-4.100}
Frequency (Hz)	126.320 [±38.370]; 130.000 {60.000-180.000}
Pulse width (us)	68.800 [±17.635]; 60.000 {60.000-130.000}
Power of stimulation	57.289 [±31.157]; 55.608 {5.281 -121.571}

 Table 1. Stimulation parameters at postoperative evaluation.

	No. (%); mean [±SD]; median {range}				
	Preoperative assessment		Postoperative assessment	stoperative assessment	
Variable	Off-medication	On-medication	On-stimulation/off- medication	Off-stimulation/off- medication	On-stimulation/ on-medication
Speech variables					
Speech intelligibility (%)	93.04 [±8.17]; 94.00 {64.00-100.00}	92.04 [±8.37]; 94.00 {62.00-100.00}	89.52 [±15.83]; 96.00 {48.00-100.00}	84.34 [±18.00]; 94.00 {48.00-100.00}* ç	84.64 [±18.40]; 92.00 {28.00-100.00}
Mean intensity of spontane- ous speech (dB)	66.76 [±5.96]; 67.00 {59.00-86.00}	66.92 [±7.28]; 68.00 {49.00-76.00}	65.32 [±6.87]; 65.00 {52.00-81.00}	63.04 [±4.76]; 64.00 {56.00-70.00}	65.28 [±6.02]; 67.00 {54.00-74.00}
F0 SD of spontaneous speech (Hz)	35.15 [±20.09]; 31.12 {1.28-89.00}	36.81 [±18.71]; 32.17 {0.80-76.00}	35.13 [±16.12]; 31.57 {14.98-80.24}	30.03 [±16.90]; 29.49{7.84- 92.56}	32.80 [±12.74]; 31.42{13.87-63.47}
Maximum phonation time (MPT) (seconds)	14.87 [±5.38]; 14.00 {4.00-26.00}	16.48 [±5.37]; 17.00 {7.00-26.00}	15.29 [±7.00]; 13.00 {6.20-32.00}	12.30 [±5.11]; 12.00 {5.00-27.00}* [£]	13.74 [±5.47]; 13.00 {7.00-31.00}
Mean intensity of sustained phonation (dB)	73.04 [±6.89]; 72.00 {60.00-89.00}	72.24 [±7.06]; 72.00 {59.00-87.00}	68.80 [±9.16]; 70.00 {52.00-88.00}	67.32 [±7.20]; 68.00 {55.00-85.00} ^ç	69.20 [±8.90]; 71.00 {46.00-88.00}
Count rate (sill/sec)	4.92 [±1.31]; 4.75 {1.90-7.75}	4.82 [±1.47]; 4.75 {1.50-7.75}	4.28 [±1.43]; 4.25 {2.22-7.29}	4.16 [±1.16]; 4.25 {1.46-6.38}	4.86 [±1.66]; 4.64 {2.22-9.44}
Perceptual severity of dysar- thria (1–4)	3.92 [±0.27]; 4.00 {3.00-4.00}	3.96 [±0.20]; 4.00 {3.00-4.00}	$\begin{array}{c} 3.40 \ [\pm 0.70]; \ 3.00 \\ \{1.00{-}4.00\}^{\varsigma, \pounds} \end{array}$	$\begin{array}{c} 3.40 \ [\pm 0.71]; \ 4.00 \\ \{2.00{-}4.00\}^{\varsigma, \pounds} \end{array}$	$\begin{array}{c} 3.28 \ [\pm 0.67]; \ 3.00 \\ \{2.00 - 4.00\}^{\varsigma, \mathcal{E}} \end{array}$
Clinical variables					
UPDRS part I	2.04 [±1.95]; 2.00 {0.00-8.00}	-	3.00 [±2.02]; 3.00 {0.00-8.00	}	
UPDRS part II	19.92 [±5.67]; 20.00 {9.00-33.00}	7.08 [±4.53]; 7.00 {1.00-17.00}	19.28 [±5.37]; 21.00 {6.00–29.00}		13.52 [±5.73]; 14.00 {4.00-23.00}
UPDRS part-III	36.64 [±9.27]; 34.00 {25.00-62.00}	14.64 [±7.38]; 13.00 {3.00-31.00}	29.28 [±12.41]; 26.00 {13.00-58.00}	46.20 [±12.81]; 47.00 {25.00-73.00}	15.80 [±9.07]; 12.00 {5.00-38.00}
UPDRS part IV	7.13 [±2.40]; 7.00 {4.00-12.00)}	4.40 [±2.06]; 4.00 {1.00-9.00}		
Hoehn and Yahr	2.82 [±0.61]; 2.50 {2.00-4.00}	1.98 [±0.42]; 0.42 {1.00-2.50}	2.78 [±0.71]; 2.50 {2.00- 5.00}	3.64 [±1.06]; 4.00 {2.00- 5.00}	2.40 [±0.50]; 2.50 {2.00- 4.00}
UPDRS akinesia subscore	12.70 [±3.18]; 12.00 {7.00-18.00}	4.48 [±3.24]; 4.00 {0.00-12.00}	11.12 [±5.45]; 11.00{2.00- 23.00}	17.40 [±5.93]; 18.00 {4.00-28.00}	6.44 [±4.83]; 5.00 {0.00-17.00}
UPDRS tremor subscore	4.65 [±4.11]; 3.00 {0.00-14.00}	1.26 [±2.20]; 0.00 {0.00-9.00}	2.96 [±2.35]; 3.00 {0.00-7.00}	4.68 [±2.86]; 4.00 {0.00-10.00}	0.64 [±0.99]; 0.00 {0.00-4.00}
UPDRS PIGD subscore	8.13[±3.52]; 8.00 {3.00-16.00}	2.61[±1.78]; 2.00 {0.00-7.00}	7.92 [±3.06]; 8.00 {1.00-13.00}	9.40 [±3.60]; 9.00 {1.00-15.00}	5.04 [± 3.44]; 5.00 {0.00-12.00}
UPDRS item 18	1.347 [±0.57]; 1.00 {0.00-2.00}	0.608 [±0.65]; 1.00 {0.00-2.00}	1.52 [±0.71]; 1.00 {1.00-3.00}	1.68 [±0.74]; 2.00 {1.00-3.00}	1.44 [±0.65]; 1.00 {0.00-3.00}
LEDD (mg)	925.10 [±439.522]; 1045.00 {2	200.00-1898.00}	817.36 [±358.499]; 807.00 {118.00-1500.00}		
Phonemic fluency	34.47 [±7.26]; 34.22 {18.29-4	6.90}	27.66 [±10.57]; 27.85 {9.75–57.18}		
Spatial perception localiza- tion of numbers	8.55 [±1.13]; 9.00 {7.00-10.00)}	7.81 [±8.00]; 8.00 {3.00-10.00	0}	
1947 colored Raven's pro- gressive matrices	28.78 [±4.34]; 30.24 {21.00-3	5.61}	24.93 [±5.79]; 24.59 {16.84-40.52}		
Stroop test "time"	20.07 [±11.45]; 17.70 {8.00-4	7.00}	27.51 [±19.60]; 25.12 {6.50-91.50}		
Stroop test "errors"	0.51 [±0.65]; 0.37 {0.00-2.25}		2.70 [±4.77]; 0.12 {0.00-15.7	2.70 [±4.77]; 0.12 {0.00-15.75}	
Trail making test part B	101.77 [±55.76]; 85.50 {33.00	-274.00}	168.64 [±131.24]; 120.00 {27.	.00-531.00}	

Table 2. Changes of speech and clinical variables over time. Speech variables: Friedman Test followed by Wilcoxon signed rank test post-hoc. *LEDD* L-dopa equivalent daily dose, *MRI* magnetic resonance imaging, *PD* Parkinson disease, *PIGD* dominant postural instability and gait disorder, *SD* standard deviation, *UPDRS* Unified Parkinson's Disease Rating Scale. *p-value < 0.005 with respect to the on-stimulation/off-medication condition. ^cp-value < 0.005 with respect to the off-medication condition. ^ep-value < 0.005 with respect to the on-medication condition.

a "stable" subgroup, "worsened" patients showed a greater preoperative and postoperative disease motor severity quantified by: (i) higher scores in the UPDRS part III total score, H&Y staging, and akinesia subscore in the off-medication condition; (ii) lower loudness of spontaneous speech and lower speech intelligibility in all three postoperative conditions; (iii) lower intensity of prolonged phonation in on-stimulation/off-medication and offstimulation/off-medication conditions (Table 3). Furthermore, they showed a significantly worse performance in the preoperative Stroop test (errors) and postoperative Trail Making test B. In addition, all the GBA1-PD patients were included in the "worsened" subgroup with a trend toward significance (p=0.06) at the chi-square independence test. Disease duration, age at surgery, follow-up duration and stimulation parameters were not significantly different between the two subgroups.

Secondary outcomes. Regarding the comparison between the different speech variables in the conditions tested, a statistically significant reduction of the duration of sustained phonation was found in the



Figure 1. Changes of speech intelligibility in the stable and worsened groups.

off-stimulation/off-medication condition when compared with the on-stimulation/off-medication condition (p < 0.005) and with the preoperative on-medication condition (p < 0.005). In addition, the mean intensity of sustained phonation was significantly reduced in the off-stimulation/off-medication condition if compared with the preoperative off-medication condition (p < 0.005) highlighting the negative effects of disease progression on this acoustic parameter.

A direct correlation between the variation of speech intelligibility and tremor (p=0.026) and PIGD subscores (p=0.040) by comparing the off-stimulation/off-medication with the on-stimulation/off-medication one was also found, highlighting that the rebound of tremor and axial symptoms can worsen speech in the acute testing situation. On the contrary, no correlations were found between the variation of speech intelligibility and the changes in the different motor scores and subscores when comparing the on-stimulation/off-medication and preoperative off-medication condition. Furthermore, a negative correlation was also found in the on-stimulation/ off-medication differents with a more severely decreased movements amplitude and speed have less intelligibility. The negative correlation between speech intelligibility and akinesia subscore was also confirmed in the on-stimulation/on-medication condition (p=0.013).

Discussion

Our results add to further observations regarding the long-term effects of bilateral STN-DBS on speech in PD patients^{7,12}. Globally, the studied cohort showed a long-term maintenance of speech intelligibility after surgery, highlighting some possible beneficial long-term effects of STN-DBS when comparing off stimulation and on stimulation conditions. This is consistent with previous studies that showed no worsening of speech following STN-DBS when assessed either with the UPDRS speech item¹⁵ or dedicated perceptual assessments¹⁶, which was reduced with the introduction of L-DOPA¹⁷, in line with our findings. Nevertheless, when using a proper perceptual assessment of speech intelligibility, it is commonly accepted that a significant worsening of speech intelligibility should be expected one year after surgery, when comparing postoperative on-stimulation/offmedication condition with the preoperative off-medication condition^{9,18}. This has also been reported in the long-term by Aviles-Olmos et al.¹², who reported a significant worsening of speech intelligibility at five (-43.7%)and eight years (-21.4%) in the off-medication conditions if compared with preoperative values. The different results obtained in our cohort may be due to the different evaluation of speech intelligibility (i.e., sentence task of the Assessment of Intelligibility for Dysarthric Speech and single word intelligibility). However, by looking at the individual cases of our cohort in detail, two distinct subgroups could be identified based on the long-term changes of speech intelligibility, with different clinical characteristics. This is in line with similar approaches that tried to disentangle different possible speech outcomes following STN-DBS^{18,19}. Patients in the "worsened" subgroup showed a worse preoperative and postoperative motor disease severity together with a worse cognitive function particularly regarding executive-frontal domain. These results are in line with a recent 2-year follow-up

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ExperienceFormation and a sequence of the sequence o	Variable	"Worsened" (n=9)	"Stable/improved" (n = 16)	P value	
Se indersanie)094 (ab23)010 (ab23)010Age al Dougnely294 (ab24)040 (ab24)040 (ab24)040 (ab24)Age al Dougnely295 (ab14)040 (ab14)040 (ab14)040 (ab14)Age and program295 (ab14)040 (ab14)040 (ab14)040 (ab14)Includy regramments (%)040 (ab14)040 (ab14)040 (ab14)040 (ab14)OPDB part (ab endancian)042 (ab14)040 (ab14)040 (ab14)040 (ab14)OPDB part (ab endancian)042 (ab14)040 (ab14)040 (ab14)040 (ab14)OPDB part (ab endancian)040 (ab14)040 (ab14)040 (ab14)040 (ab14)OPDB part (ab14)040 (ab14)040 (a	Preoperative variable		I		
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App and supproprimation of the structure	Age at PD onset (years)	49.44 [±5.54]; 48.00 {41.00-57.00}	46.81[±5.62]; 46.50 {38.00-55.00}	0.201	
Dense namin at negar (van)08/14 (100, 100, 100, 100)0007 (150, 100, 100, 100, 100)015Lendopa regonations (0)04/14 (100, 100, 100, 100, 100, 100, 100, 100	Age at surgery (years)	59.55 [±4.15]; 60.00 {54.00-65.00}	57.75 [±6.48]; 58.50 {46.00-71.00}	0.378	
Investor61.41 (-20.9) (-60.1940-9.200)60.01 (-1.11) (-0.01, -000)53.2LDD (ng)9273 (-77.211100 (1500-01800)10.01 (-27.91) (1200 (1500-01800)0.01UPDRS part III of medication15.21 (-1.04 (-1.50.0 (-1.000), -2.01 (-0.04 (-1.50.0 (-0.000), -0.00))0.01UPDRS diames induces of medication15.51 (-2.01 (-1.50.0 (-1.500), -2.000), -0.000.00UPDRS diames induces of f-medication15.51 (-2.01 (-1.500), -0.00, -0.00)0.00UPDRS diames induces of f-medication15.51 (-2.01 (-0.01 (-0.000), -0.00), -0.000.00UPDRS diames induces of f-medication15.51 (-2.01 (-0.01 (-0.000), -0.00), -0.000.00UPDRS diames induces of f-medication15.51 (-2.01 (-0.01 (-0.000), -0.00), -0.000.00Values (CAA heterosysse matalian)21.53 (-5.00 (-0.000), -0.000, -0.0	Disease duration at surgery (years)	9.66 [±4.00]; 8.00 {5.00-16.00}	10.87 [±5.00]; 8.50 {6.00-25.00}	0.587	
LEDD (mg)997.31 [:377:41 (1040) [3500-14500)990.01 [:47.990] (1030) [:300 (1000-18500)0.419UPDIS part III (melication)1.37 [:10.66], 3.00 (12.00-14.00)1.26 [:10.06], 3.20 (200-4.00)0.051UPDIS Admins tokes of medication1.57 [:12.07], 15.00 (12.00-18.00)1.12 [:12.02], 11.00 (7.00-100)0.051UPDIS Admins tokes of medication1.57 [:12.37], 15.00 (12.00-18.00)0.0510.051UPDIS Admins tokes or emedication1.57 [:12.37], 15.00 (12.00-18.00)0.0510.051UPDIS Admins tokes or emedication1.00 [:12.00] (12.00-14.00)1.12 [:12.00 (20.00, 00)0.051Cencic analys1.12.00 [:12.00], 10.00 (12.00, 10.00)0.0510.051Partiso (15.00 (12.00, 10.00)1.051 [:12.00], 9.00 (10.00, 2.02)0.051Strong ten "error"0.061 [:12.00], 10.00 (10.00, 2.02)0.051Speech instlightify (%) of medication0.051 [:12.00], 9.00 (10.00, 2.02)0.051Speech instlightify (%) or emedication0.051 [:12.00], 9.00 (10.00, 2.02)0.072Mean intensity of quentees speech (10.00 emedication0.051 [:12.00], 9.00 (12.00, 2.00)0.021Di Speech instlightify (%) or emedication0.051 [:12.00], 10.00 (12.00, 2.00)0.021Di Speech instlightify (%) or emedication0.051 [:12.00], 10.00 (12.00, 2.00)0.021Di Speech instlightify (%) or emedication0.051 [:12.00], 10.00 (12.00, 2.00)0.021Di Speech instlightify (%) or emedication0.051 [:12.00], 10.00 (12.00, 2.00)0.021Di Speech instlightify (%) or emedication0.051 [:12.00], 10.00 (12.00, 2.00)0.021 </td <td>Levodopa responsiveness (%)</td> <td>65.14 [±20.39]; 66.00 {34.00-93.00}</td> <td>60.60 [±14.13]; 60.71 {40.00-90.00}</td> <td>0.552</td>	Levodopa responsiveness (%)	65.14 [±20.39]; 66.00 {34.00-93.00}	60.60 [±14.13]; 60.71 {40.00-90.00}	0.552	
UPDR Spreak31.21 [± 0.41]; 4.00 [15.00-4.00]31.91 [± 4.24]; 2.20 (-9.00)0.016Ibech and War of medication1.53 [± 2.27]; 15.00 [2.00-18.00]1.53 [± 2.24]; 1.10 [7.00-18.00]0.051UPDRS Alumis ablacer of medication6.57 [± 3.39]; 5.00 [1.00 ± 2.00]3.47 [± 2.4]; 3.00 [0.0-0.0]0.054UPDRS Alumis ablacer of medication1.00 [± 2.57]; 10.00 [5.00-18.00]7.15 [± 2.4]; 3.00 [0.0-0.0]0.054UPDRS Alumis ablacer of function1.000 [± 7.50]; 10.00 [5.00-18.00]7.15 [± 2.4]; 3.00 [0.00-2.0]0.054VDPRS FLO Subscore of function1.000 [± 7.50]; 10.00 [5.00-18.00]0.0510.054Paultie (GRA heteorygous matation)0.01 [± 0.65]; 0.57 [5.00-2.00]0.021 [± 0.65]; 0.01 [0.00]; 10.00 [1.00 ± 2.57]0.025Serech intelligibility (%) of medication8.11 [± 1.01]; 4.00 [± 0.0-10.00]9.15 [± 4.25]; 5.00 [1.00]0.075Mean intensity of portaneous speech (H2) of medication6.61 [± 0.31]; 5.00 [1.00]; 0.00 [1.00 ± 2.57]0.054BS Of oportaneous speech (H2) of medication3.02 [± 2.07]; 0.01 [± 2.57]; 0.00 [0.00 ± 7.00]0.054BS Of oportaneous speech (H2) of medication3.02 [± 2.07]; 0.01 [± 5.57]; 0.02 (0.00]0.054BV Sof oportaneous speech (H2) of medication3.02 [± 2.07]; 0.01 [± 5.57]; 0.02 (0.00]0.054BV Sof oportaneous speech (H2) of medication3.02 [± 2.07]; 0.02 (1.00]0.054BV Sof oportaneous speech (H2) of medication3.02 [± 2.07]; 0.02 (0.00]0.02 [± 0.07]BV Sof oportaneous speech (H2) of medication3.02 [± 2.07]; 0.02 (0.00]0.02 [± 0.07]; 0.02 (0.00]BV Sof oportan	LEDD (mg)	987.33 [±377.74]; 1104.00 {350.00-1405.00}	890.09 [±478.90]; 1023.00 {200.00-1898.00}	0.419	
Isolan adula of analoxion12 17 (19.06); 200 (29-1.00)26 12 09(1; 201 (201-00)0.039UPDS datasis subscor of medication15.50 (12.07); 15.00 (12.00-1.800)11.20 (12.02); 11.00 (12.00-1.800)0.040UPDS datasis subscor of medication10.00 (12.50); 15.00 (12.00-1.800)7.13 (2.30); 10.00 (10.00-1.800)0.040UPDS false subscor of medication10.00 (12.50); 10.00 (15.00 (10.00-1.800)0.0400.040Centric analysis6.66 (70%)10.100 (0%)0.010Seege in analysis (10.00 (10	UPDRS part-III off-medication	43.22 [±10.41]; 45.00 {31.00-62.00}	32.94 [±6.24]; 32.50 {25.00-49.00}	0.016	
UPDS Alexista obscore of medication15.91 (± 2017): 16.00 (12.00–16.00)10.012 (± 2.012): 10.00 (000–6.00)00.02UPDS Riel obscore of medication6.37 (± 2.012): 10.00 (52.0–16.00)7.13 (± 2.012): 10.00 (000–6.00)0.036Ortpos Riel obscore of medication0.001 (± 2.701): 10.00 (52.0–16.00)7.13 (± 2.012): 20.00 (000–6.00)0.036Negative0.0050.0050.0050.0050.005Negative0.016 (10.000–5.201)0.33 (± 0.001; 0.00 (0.00–2.201)0.035Speech intelligibility (%) of medication80.11 (± 1.012): 40.00 (0.00–100.00)9.52 (± 5.20; 9.7.00 (12.00–100.00)0.075Speech intelligibility (%) of medication81.1 (± 1.012): 40.00 (0.00–100.00)9.52 (± 5.20; 9.7.00 (12.00–100.00)0.075Speech intelligibility (%) of medication81.1 (± 7.018; 0.600 (1500–05.00)0.051 (± 2.00; 0.550 (1500–7.00)0.052Speech intelligibility (%) on medication3.041 (± 1.012): 40.00 (0.00–100.00)9.52 (± 2.00; 0.00–7.00)0.052Speech intelligibility (%) on medication3.041 (± 1.012): 40.00 (0.00–10.00)9.52 (± 2.00; 0.00–7.00)0.052Speech intelligibility (%) on medication3.041 (± 0.01; 0.00)0.051 (± 0.00)0.052Speech intelligibility (%) on medication3.015 (± 1.012): 40.00 (0.00)1.051 (± 0.00): 40.000.052Speech intelligibility (%) on medication3.015 (± 1.012): 40.00 (0.00)1.051 (± 0.00): 40.000.052Speech intelligibility (%) on medication1.511 (± 1.012): 40.01 (0.00–10.00)1.551 (± 0.00): 40.000.052Speech intelligibility (%) on medication <td< td=""><td>Hoehn and Yahr off-medication</td><td>3.17 [±0.66]; 3.00 {2.50-4.00}</td><td>2.63 [±0.50]; 2.50 {2.00-4.00}</td><td>0.038</td></td<>	Hoehn and Yahr off-medication	3.17 [±0.66]; 3.00 {2.50-4.00}	2.63 [±0.50]; 2.50 {2.00-4.00}	0.038	
IPPBS kinesis abserse n-neckacian6.77 [1.3 wp]: 501 [1.00-12.00]4.71 [1.2 kp]: 501 (0.00-8.00]0.049UPDBS IPIGD subscore off-medication10.00 [1.2 xp]: 1.000 [1.20-16.00]7.13 [1.2 kp]: 7.01 (0.00-15.00]0.060Cencic analyz6 (6.6 7ms)16 (100.00m)0.00Pasitive (GBA heterscoppen mutation)3.31 (0.061 (0.00-2.27)0.031Strops for Terns ⁿ 0.81 [1.0 kp]: 6x0 (0.00-0.000]9.52 [1.5 2x0]; 7.00 (0.20-0.100]0.102Speech intilligibility (0.01 -medication65.51 [1.1 kg]: 4x0 (0.20-0.1000)9.52 [1.4 kg]: 55.00 (0.40-0.1000)0.75Man intensity of spontancous speech (BD) on-medication66.11 [1.2 xB]: 6.800 [1.90-0.500]66.00 [1.4 cg]: 6.8 (0.500-0.000]0.75Nan intensity of spontancous speech (BD) on-medication3.41 [1.6 kg]: 4.941 [2.20-6.16 kg]3.51 [1.2 201]: 4.001 (0.00-2.000)0.42PD SD of spontancous speech (BD) on-medication1.41 [1.4 kg]: 4.00 (7.00-1.001)1.47 [1.2 kg]: 4.801 (8.00-2.000)0.42Natizumu phonation time (MT) (1.0 on-medication7.41 [1.4 kg]: 7.201 (0.60-7.000)1.75 [1.5 kg]: 1.851 (0.60-2.000)0.42Natizumu phonation time (MT) (1.0 on-medication7.13 [1.4 kg]: 4.201 (7.00-1.001)1.75 [1.5 kg]: 1.851 (0.60-2.001)0.82Natizumu phonation time (MT) (1.0 on-medication7.13 [1.2 kg]: 4.201 (2.00-7.000)2.78 [1.6 kg]: 2.00 (1.00-7.000)0.72Natizumu phonation time (MT) (1.0 on-medication7.13 [1.4 kg]: 4.00 (7.00-7.000)3.98 [1.2 kg]: 4.801 (3.00-7.001)0.87Natizumu phonation time (MT) (1.0 off-scillation1.81 [1.2 kg]: 4.001 (3.00-0.001)0.72	UPDRS akinesia subscore off-medication	15.50 [±2.07]; 15.00 {12.00-18.00}	11.20 [±2.62]; 11.00 {7.00–16.00}	0.002	
UPDS 9D: subsence of madication10.00 [+ 3.70]; 10.00 [300-16.00]7.13 [+ 1.92]; 7.00 [3.00-15.00]0.006Centric analysis6(66.70%)16 (100.00%)0.050Positive (GA hereorygues mutations)3 (33.50%)0.00%)0.00%)Store bit Trents"0.31 [-6.60]; 0.75 (0.00-2.00)0.33 [-6.60]; 0.00 [-0.02-25]0.055Speech intelligibility (%) of medication85.1 [-1.14]; 9.00 [-0.00,-1000095.3 [-5.30]; 9.00 [-0.00,-000]0.075Speech intelligibility (%) of medication64.11 [-7.30]; 6.600 [9.00-75.00]64.05 [+2.55]; 6.90 (0.00,-0000]0.455Speech intelligibility (%) of medication64.16 [+3.53]; 6.600 [9.00-75.00]64.05 [+2.50]; 9.200, 7.310]0.452DS of optimateous speech (HJ) of medication39.12 [+1.29]; 1.400 [2.00-61.47]33.51 [=2.200; 31.11 [1.28-89.00]0.452DS of optimateous speech (HJ) of medication13.15 [+1.44]; 1.500 [-2.00-200]14.72 [+5.56]; 1.810 [-2.00]; 31.11 [1.28-89.00]0.452Maximum phonation time (MPT) (-0) or medication7.24 [+1.24]; 1.500 [-2.00-200]17.52 [+5.56]; 1.800 [-2.00-27.00]0.842Maximum phonation time (MPT) (-0) or medication7.24 [+1.24]; 7.100 [-2.00]7.35 [+2.36]; 7.100 [-2.00]0.672Foregrala everity of dystriftin (1-0) differedication7.24 [+1.24]; 7.100 [-2.00]7.35 [+2.36]; 7.100 [-2.00]0.772Perceptual everity of dystriftin (1-0) differedication3.8 [+0.33]; 4.00 [3.0-4.00]0.121UPDS part. If of medication7.07 [+1.53]; 4.20 [-2.00]0.754 [+1.23]; 4.20 [-2.00]0.774Perceptual everity of dystriftin (1-0) differedication<	UPDRS akinesia subscore on-medication	6.37 [±3.89]; 5.00 {1.00-12.00}	3.47 [±2.42]; 3.00 {0.00-8.00}	0.054	
Genetic analysis 6 (66.70%) 16 (100.00%) 0.660 Negative 6 (66.70%) 16 (100.00%) 0.660 Stroop text "trees" 0.81 [26.85], 0.75 (10.00–2.00] 0.35 [26.91,000 (0.00–2.25]) 0.035 Stroop text "trees" 0.81 [26.85], 0.75 (10.00–10.000] 9.52 [55.20]; 97.00 [82.00–10.000] 0.022 Speech inticity/(0.90) on medication 66.61 [17.81], 40.90 (62.00–10.000] 9.52 [55.20]; 97.00 [82.00–10.000] 0.023 Maan intensity of opartanecous speech (140) on medication 66.1 [19.33], 66.00 [94.00–7.500] 66.00 [14.76], 65.50 [95.00–7.600] 0.455 DV 30 opartanecous speech (142) on medication 15.41 [11.81], 94.04 [22.00–61.83] 33.51 [12.12.21], 98.00 [0.00–7.000] 0.452 Maximum phonation time (MPT) (5) on medication 12.41 [12.81], 14.10 [80-2.500] 12.73 [14.52]; 12.12 [3.80 (10.00–7.00] 0.452 Maximum phonation time (MPT) (5) on medication 12.13 [14.21]; 14.00 [80-8.00] 17.36 [14.52]; 13.81 (400–26.00] 0.872 Count rate (160) of medication 13.13 [12.21]; 40.00 [3.00–8.00] 73.71 [4.52]; 13.06 [3.00–8.00] 0.371 [4.52]; 13.06 [3.00–8.00] 0.371 [4.52]; 13.00 [3.00–3.70] 0.892 Count rate (100) of medication 13.35 [12.21]; 40.00 [3.	UPDRS PIGD subscore off-medication	10.00 [± 3.70]; 10.00 {5.00-16.00}	7.13 [±3.09]; 7.00 {3.00-15.00}	0.060	
Negative 6 (66.70%) 16 (100.0%) 0.059 Positive (GRA heterorygous mutations) 3 (33.0%) 0 (0%) 0 (0%) 0 (0%) Strop test "reno" 0.81 [1 6.05], 0.75 (0.00–2.00) 0.53 [1 6.00], 0.00 (0.0–2.25) 0.055 Speech intellighbility (%) of medication 87.11 [1 1.149, 100 (0.00, 0.000) 95.25 [1 2.49, 1900 (0.000) 0.075 Mean intensity of gontaneous speech (10) of medication 64.61 [1 7.20], 64.00 [90.07-50.001 68.81 [1 7.40], 66.00 [90.07-50.001 0.475 DS D of spontaneous speech (112) of medication 64.61 [1 2.53], 66.00 [90.07-50.001 68.81 [1 2.200], 11.11 [1.28-80.00] 0.482 Maximum phonation time (MPT) (10) of medication 15.11 [1.430, 100.02-6.600] 14.72 [1.567, 11.85 1400-2.600] 0.482 Maximum phonation time (MPT) (10) of medication 15.11 [1.431, 14.00 [80.0-5.601] 14.73 [1.567, 11.85 1400-2.600] 0.482 Maximum phonation time (MPT) (10) of medication 15.11 [1.431, 10.00 [0.00-7.800] 17.24 [1.560], 18.00 [0.00-7.800] 0.492 Court rate (101/0) of medication 15.11 [1.442], 14.00 [0.00-7.800] 17.24 [1.560], 18.00 [0.00-7.800] 0.609 Court rate (101/0) of medication 15.11 [1.442], 10.40 [0.00-7.800] 27.21 [1.768]	Genetic analysis		I		
Postory (GA heterorygans mutations) 3(33.9%) 0.031 [= 0.63]; 0.001 (0.00-2.25] 0.033 Stroup test "errors" 0.031 [= 0.65]; 0.075 (0.001-0.000) 95.25 [: 52.09]; 97.00 (82.00-100.00) 0.012 Speech mellightility (%) of medication 87.15 [: 1.103]; 94.00 (64.00-100.00) 95.25 [: 15.20]; 97.00 (82.00-100.00) 0.76 Mare intensity of pontaneous speech (dB) of medication 64.61 [: 95.5]; 64.01 (90.00-2.05) 66.00 [: 4.76]; 65.00 (90.07.00) 0.76 Maximensity of pontaneous speech (dB) of medication 83.44 [: 16.43]; 50.40 (49.00-7.500) 65.35 [: 12.24]; 82.00 (80.00-8.00) 65.35 [: 12.24]; 82.00 (80.00-8.00) 65.35 [: 12.24]; 82.00 (80.07.00) 0.35 Maximum phonaton time (MPT) (o) off-medication 15.11 [: 15.11]; 14.101 (80.00-3.000) 14.73 [: 15.67]; 18.81 (40.0-2.000) 0.97 Maximum phonaton time (MPT) (o) off-medication 7.31 [: 16.21]; 7.401 (62.00-7.500) 7.25 [: 15.601; 18.07]; 7.00 (20.00-7.500) 0.97 Maximum phonaton time (MPT) (o) off-medication 7.31 [: 16.21]; 7.401 (62.00-7.500) 7.25 [: 15.601; 8.501; 7.00 (20.00-7.500) 0.88 Court rate (illic) off-medication 7.31 [: 16.21]; 7.401 (62.00-7.500) 7.25 [: 15.20]; 8.01 (0.00-7.57) 0.38 Court rate (illic) off-medication 7.31 [: 16.31]; 4.04 (15.0	Negative	6 (66.70%)	16 (100.00%)	0.060	
Stroop test "error" 0.81 [± 0.051 0.75 (0.00–2.00) 0.33 [± 0.061 , 0.00 (0.00–2.25) 0.035 Speech intelligibility (%) of medication 89.11 [± 11.051 ; 94.00 (64.0–100.001) 95.25 [± 3.21 ; 97.00 (82.0–100.001) 0.102 Speech intelligibility (%) of medication 89.11 [± 71.051 ; 64.00 (64.00–100.01) 94.56 [± 3.251 ; 65.00 (84.00–100.00] 0.075 Mean intensity of spontaneous speech (18) of medication 84.11 [± 7.291 ; 64.00 (9400–75.00) 64.81 [± 5.751 ; 64.00 (9400–75.00) 0.485 PS D of spontaneous speech (17) of medication 39.71 [± 12.971 ; 40.87 (22.0–61.47) 35.35 [± 22.041 ; 28.00 (8.0.0–76.00) 0.384 Maximum phonation time (MPT) (5) on medication 11.515.131; 14.104 (800–26.00) 14.75 [± 5.501 ; 15.80 (7.00–26.00) 0.977 Mean intensity of sustained phonation (28) of medication 71.31 [$\pm 6.127, 17.00$ (62.00–78.00) 72.75 [$\pm 7.681; 7.200$ (50.0–87.00) 0.977 Perceptual security of dyaarthria (1–4) of medication 73.8 [$\pm 0.331, 4.00$ (20.0–78.00) 72.75 [$\pm 7.681; 7.200$ (50.0–87.00) 0.777 Perceptual security of dyaarthria (1–4) of medication 73.8 [$\pm 0.231, 4.00$ (20.0–400) 0.331 [$\pm 0.231, 4.00$ (20.0–400) 0.812 VDPDS part-110 on-medication 72.47 [$\pm 7.491, 72.00$ (62.0–28.00) 12.94 [$\pm 4.$	Positive (GBA heterozygous mutations)	3 (33.30%)	0 (0%)		
Speech intellighting (%) off-medication 89.11 [±11.05]; 94.00 [64.00-100.00] 95.25 [±5.20]; 97.00 [82.00-100.00] 0.012 Speech intellighting (%) on medication 67.55 [±11.34]; 90.00 [62.00-100.00] 95.65 [±4.57]; 55.00 [\$4.00-100.00] 0.075 Mean intensity of spontaneous speech (4B) off-medication 64.61 [±9.35]; 65.00 [9300-75.00] 66.00 [±4.76]; 65.05 [\$300-75.00] 0.405 P0 SD of spontaneous speech (1D) off-medication 38.11 [±7.80]; 65.00 [\$40.00-75.00] 63.18 [±5.78]; 68.50 [\$50.00-75.00] 0.402 P0 SD of spontaneous speech (1D) off-medication 15.11 [±1.31]; 14.00 [800-26.00] 14.72 [±5.67]; 13.85 [4.00-26.00] 0.462 Maximum phonation time (MPT) (s) off-medication 72.41 [±7.40]; 7.00 [60.00-78.00] 72.75 [±5.86]; 18.01 [7.00-75.00] 0.462 Count rate (idl/s) of-medication 72.44 [±7.40]; 7.00 [60.00-78.00] 72.75 [±5.87]; 72.00 [50.00-87.00] 0.697 Count rate (idl/s) on-medication 14.12 [=2.12]; 4.64 [±2.50-6.33] 48.8 [±1.62]; 4.82 [±5.0-7.75] 0.377 Perceptual severity of dysarthira (1-4) off-medication 38.8 [±0.33]; 4.00 [500-72.00] 3.61 [±0.20]; 4.00 [±0.0-10.00] 0.032 Perceptual severity of dysarthira (1-4) off-medication 38.8 [±0.33]; 4.00 [500-72.00] 2.56 [±5.63]; 13.00 [3.00-2.00] <td< td=""><td>Stroop test "errors"</td><td>0.81 [±0.65]; 0.75 {0.00-2.00}</td><td>0.33 [±0.60]; 0.00 {0.00-2.25}</td><td>0.035</td></td<>	Stroop test "errors"	0.81 [±0.65]; 0.75 {0.00-2.00}	0.33 [±0.60]; 0.00 {0.00-2.25}	0.035	
Speech intelligibility (%) on medication 87.55 [±11.34]; 90.09 (62.00-100.00] 94.56 [±4.95]; 95.00 [84.00-100.00] 0.075 Mean intensity of spontaneous speech (dB) on-medication 64.61 [±3.35]; 68.00 [9400-75.00] 66.01 [±3.55]; 68.00 [55.00-76.00] 0.452 PDS D of spontaneous speech (dB) on-medication 35.41 [±7.48]; 63.00 [9400-75.00] 65.11 [±3.78]; 40.00 [63.07-6.00] 0.842 PDS D of spontaneous speech (H2) on-medication 13.11 [±1.33]; 14.10 [80.09-2.6.00] 14.77 [±5.57]; 13.85 [40-2.6.00] 0.842 Maximum phonation time (MT) (0 on medication 14.35 [±4.44]; 15.00 [7.00-21.00] 17.55 [±5.66]; 18.50 [7.00-26.00] 0.977 Mean intensity of sustained phonation (BD) on-medication 72.44 [±7.40]; 73.00 (60.00-78.00) 72.75 [±2.08]; 72.00 [50.00 7.70.0] 0.607 Count rate (all/a) off-medication 45.1 [±0.34]; 4.73 [1.00-5.77] 50.8 [±1.47]; 4.50 (15.00-7.87] 0.380 Count rate (all/a) off-medication 3.38 [±0.33]; 4.00 [3.00-4.00] 3.91 [±0.25]; 4.20 (15.00-7.80] 0.673 Perceptual severity of dyarthria (1-4) on-medication 3.88 [±0.33]; 4.00 [3.00-4.00] 3.91 [±0.25]; 4.00 [5.00-4.00] 0.612 PUPRS part-10 m-stimulation/off-medication 1.67 [±0.52]; 2.200 (6.00-2.800] 1.52 [±0.46]; 1.100 [3.00-4.00] 0.612 </td <td>Speech intelligibility (%) off-medication</td> <td>89.11 [±11.05]; 94.00 {64.00-100.00}</td> <td>95.25 [±5.20]; 97.00 {82.00-100.00}</td> <td>0.102</td>	Speech intelligibility (%) off-medication	89.11 [±11.05]; 94.00 {64.00-100.00}	95.25 [±5.20]; 97.00 {82.00-100.00}	0.102	
Mean intensity of spontaneous speech (dB) off-medication 68.11 [±7.80]; 68.00 [99.00-86.00] 66.00 [±4.76]; 65.50 [99.00-73.00] 0.776 Mean intensity of spontaneous speech (dB) on-medication 64.66 [±9.35]; 68.00 (±9.00-75.00] 66.00 [±4.76]; 65.50 [95.00-76.00] 0.462 POS D of spontaneous speech (H2) on-medication 39.71 [±1.20]; 40.87 [22.10-61.47] 53.51 [±2.20]; 80.00 [4.00-26.00] 0.432 Maximum phonation time (MPT) (i) off-medication 15.11 [±5.13]; 14.00 [80.0-26.00] 17.56 [±5.66]; 15.90 [7.00-26.00] 0.462 Maximum phonation time (MPT) (i) on-medication 72.41 [±7.40]; 15.00 [7.00-27.00] 17.56 [±5.66]; 15.90 [7.00-26.00] 0.472 Mean intensity of sustained phonation (dB) on-medication 72.41 [±7.40]; 73.00 [60.00-78.00] 73.77 [±6.83]; 71.90 (50.00-87.00] 0.679 Count rate (all/k) on-medication 47.8 [±0.33]; 4.00 [3.00-4.00] 3.83 [±0.23]; 4.00 [3.00-4.00] 0.673 Perceptual severity of dyarthria (1-4) on-medication 3.88 [±0.33]; 4.00 [3.00-4.00] 4.09 [±0.0]; 4.00 (4.00-4.00] 0.182 Postoperative variable UPDRS part-110 on-timulation/off-medication 2.66 [±0.59]; 2.300 (13.00-3.600] 0.031 UPDRS part-110 on-timulation/off-medication 2.16 [±1.71]; 1.20 [±0.00-2.400] 1.512 1.56 [±1.71]; 1	Speech intelligibility (%) on-medication	87.55 [±11.34]; 90.00 {62.00-100.00}	94.56 [±4.95]; 95.00 {84.00-100.00}	0.075	
Mean intensity of spontaneous speech (Hz) off-medication 64.66 [±9.35], 68.00 [19.00-75.00] 68.18 [±5.78], 68.50 [55.00-76.00] 0.452 FO SD of spontaneous speech (Hz) off-medication 38.47 [±1.643], 30.44 [22.88-61.63] 33.51 [±2.201, 31.11 [12.8-99, 00] 0.462 FO SD of spontaneous speech (Hz) off-medication 39.72 [±1.297], 49.77 [21.00 -12.00] 17.75 [±5.66], 18.50 [7.00-26.00] 0.842 Maximum phonation time (MPT) (s) off-medication 12.41 [±4.41], 15.00 [7.00-21.00] 17.75 [±5.66], 18.50 [7.00-26.00] 0.977 Mean intensity of sustained phonation (Hz) off-medication 7.44 [±7.447, 17.00 (62.00-78.00] 7.37 [±6.32], 7.10 (50.00-87.00] 0.977 Mean intensity of sustained phonation (Hz) off-medication 7.34 [±6.32], 7.400 (62.00-78.00] 7.275 [±7.68], 72.00 (59.00-87.00] 0.677 Court at (sill/s) off-medication 4.58 [±0.29], 4.75 [1.00-56.77] 0.380 [±0.21], 4.92 (±0.29], 4.75 [±0.05 [±0.01 (3.00-4.00] 0.677 Pactopatia severity of dyarthria (1-4) off-medication 3.88 [±0.33], 4.00 (3.00-4.00] 3.91 (±0.21], 4.22 (±0.53) 0.91 ±0.01 (±0.01, 4.00 (±0.00-4.00) 0.021 UPDRS part-II off-medication 2.16 (±1.31, 2.20 (±0.01, 3.00) 1.21 (±5.44, 1.20 (±0.01, 3.00) 0.021 0.021 0.021 0.021 0.021	Mean intensity of spontaneous speech (dB) off-medication	68.11 [±7.80]; 68.00 {59.00-86.00}	66.00 [±4.76]; 65.50 {59.00–73.00}	0.776	
PB Do fopontaneous speech (Hz) off-medication 38.41 [±16.43]; 30.44 [22.68=f1.63] 33.51 [±22.0]; 31.11 [1.28=49.00] 0.462 PO SD of spontaneous speech (Hz) on-medication 37.27 [±1.27]; 0.407 [21.0=1.47] 35.55 [±21.24]; 29.00 (8.08=7-6.00) 0.358 Maximum phonation time (MPT) (s) on-medication 14.55 [±4.44]; 15.00 (7.00=2.00) 17.56 [±5.66]; 13.85 [4.00=26.00] 0.452 Maximum phonation time (MPT) (s) on-medication 72.44 [±7.40]; 73.00 (60.0=8.00) 73.57 [±6.82]; 71.00 (50.00=87.00) 0.690 Count ate (all/s) of-medication 4.61 [±0.94]; 4.75 [3.00=5.67] 5.08 [±1.47]; 4.97 (190=7.75) 0.777 Perceptual severity of dysarthria (1=4) off-medication 4.73 [±1.23]; 4.64 (2.50=6.33) 4.86 [±1.62]; 4.20 (19.0=7.05) 0.782 Perceptual severity of dysarthria (1=4) on-medication 3.88 [±0.33]; 4.00 (3.00=4.00) 4.00 [±0.00]; 4.00 (4.00=4.00) 0.152 Potoperative variable UPDRS part-II off-medication 2.67 [±6.32]; 2.00 (14.00=5.800) 2.45 [±6.57]; 2.00 (14.00=5.800) 2.45 [±6.57]; 2.00 (14.00=5.800) 2.45 [±6.57]; 2.00 (14.00=5.800) 0.052 UPDRS part-II on-stimulation/off-medication 1.52 [±6.46]; 17.00 (3.00=4.00) 6.031 0.012 0.012 UPDRS part-II on-stimulation/off-medication <td< td=""><td>Mean intensity of spontaneous speech (dB) on-medication</td><td>64.66 [±9.35]; 68.00 {49.00-75.00}</td><td>68.18 [±5.78]; 68.50 {55.00–76.00}</td><td>0.495</td></td<>	Mean intensity of spontaneous speech (dB) on-medication	64.66 [±9.35]; 68.00 {49.00-75.00}	68.18 [±5.78]; 68.50 {55.00–76.00}	0.495	
P6 BD of spontaneous speech (H2) on-medication 39.72 [±12.97]; 40.87 [22.10-61.47] 35.35 [±21.24]; 20.00 [0.80-76.00] 0.358 Maximum phonation time (MPT) (s) off-medication 15.11 [±5.13]; 14.00 [80.00-26.00] 14.75 [±5.67]; 15.38 [4.00-26.00] 0.452 Maximum phonation time (MPT) (s) off-medication 72.44 [±7.40]; 73.00 (60.00-86.00] 73.37 [±6.82]; 71.50 (63.00-89.00] 0.692 Count rate (sill/s) off-medication 71.34 [±6.12]; 74.00 (20.00-7.800] 72.75 [±7.68]; 72.00 (59.00-87.00] 0.690 Count rate (sill/s) off-medication 4.61 [±0.49]; 4.75 [13.00-5.67] 508 [±1.74]; 4.97 [140-7.75] 0.330 Count rate (sill/s) off-medication 3.88 [±0.33]; 4.00 [3.00-4.00] 3.93 [±0.25]; 4.00 [3.00-4.00] 0.693 Perceptual severity of dysarthria (1-4) off-medication 3.88 [±0.33]; 4.00 [3.00-4.00] 3.00 [±0.00]; 4.00 [±0.00]; 4.00 [±0.00] 0.073 Perceptual severity of dysarthria (1-4) off-medication 2.167 [±6.32]; 2.300 (6.00-29.00] 1.794 [±4.42]; 18.50 [9.00-24.00] 0.023 UPDRS part-III on-stimulation/off-medication 1.567 [±0.200 [±0.00-88.00] 1.251 [±4.42]; 1.100 [±0.00-24.00] 0.017 UPDRS skinesia subscore, on-stimulation/off-medication 1.576 [±5.63]; 1.000 (±0.00-28.00] 1.584 [±4.23]; 1.680 [±0.00]; 1.000 [±0.00]	F0 SD of spontaneous speech (Hz) off-medication	38.41 [±16.43]; 30.44 {22.68-61.63}	33.51 [±22.00]; 31.11 {1.28-89.00}	0.462	
Maximum phonation time (MPT) (s) off-medication 15.11 [±5.13]; 14.00 [8.00–26.00] 14.73 [±5.67]; 13.85 [4.00–26.00] 0.842 Maximum phonation time (MPT) (s) on-medication 14.55 [±4.41]; 15.00 (7.00–21.00] 17.56 [±5.66]; 18.50 (7.00–26.00] 0.165 Mean intensity of sustained phonation (dB) off-medication 7.13 [±6.12]; 7.40 (62.00–78.00] 7.37 [±6.82]; 7.150 (63.00–89.00] 0.699 Court rate (sIII/s) off-medication 4.15 [±0.31]; 4.00 (62.00–86.00] 7.37 [±6.82]; 7.10 (63.00–89.00] 0.699 Court rate (sIII/s) off-medication 4.15 [±0.31]; 4.40 (25.00–5.67] 5.08 [±1.47]; 4.97 [1.90–7.75] 0.380 Court rate (sIII/s) off-medication 3.88 [±0.33]; 4.00 (3.00–4.00] 3.53 [±0.23]; 4.00 (3.00–4.00] 0.673 Preceptual severity of dysarthria (1–4) on-medication 2.167 [±5.52]; 2.3.00 (5.00–7.9.00] 1.794 [±4.42]; 18.50 (9.00–24.00] 0.637 UPDRS part-III on-stimulation/off-medication 2.167 [±5.76]; 4.200 [14.00–8.8.00] 2.31 [±5.42]; 1.100 (5.00–24.00] 0.011 UPDRS skinesia subscore, off-stimulation/off-medication 2.001 [±1.71]; 2.200 [±0.0–23.00] 8.81 [±3.03]; 0.00 [±0.0–10.00] 0.81 UPDRS skinesia subscore, off-stimulation/off-medication 2.001 [±1.7.2]; 2.001 (4.00–8.8.00] 1.23 [±5.42]; 1.100 (5.00–7.00]	F0 SD of spontaneous speech (Hz) on-medication	39.72 [+12.97]: 40.87 {22.10-61.47}	35.35 [+21.24]: 29.00 {0.80-76.00}	0.358	
Maximum phonation time (MPT) (s) on medication 1452 [24.44]; 15.00 (7.00–21.00) 7.55 [25.66]; 18.50 (7.00–26.00) 0.165 Mean intensity of sustained phonation (dB) off-medication 7.244 [27.40]; 7.300 (62.00–86.00) 7.37 [16.82]; 7.200 (53.00–87.00) 0.609 Count rate (sill/s) off-medication 7.13 [26.12]; 7.400 (62.00–87.00) 7.275 [27.68]; 7.200 (53.00–87.00) 0.609 Count rate (sill/s) off-medication 4.16 [20.94]; 4.75 [3.03–65.77) 5.081 [4.7]; 4.57 [1.80–7.75] 0.830 Count rate (sill/s) on-medication 4.73 [21.23]; 4.64 [25.0–6.33] 4.86 [21.62]; 4.82 [1.50–7.75] 0.777 Perceptual severity of dysarthria (1–4) on-medication 3.88 [20.33]; 4.00 [3.00–4.00] 3.93 [20.25]; 4.00 [3.00–4.00] 0.812 Postperative variable 2.06 [21.30]; 2.200 [3.00–4.00] 1.794 [24.42]; 1.8.0 [9.0–2.400] 0.017 UPDRS part-III on-stimulation/ofm-medication 2.200 [11.13]; 2.200 [5.00–3.800] 1.231 [25.42]; 1.100 (5.00–2.400] 0.017 UPDRS satinesis subscore, on-stimulation/off-medication 2.764 [2.50]; 1.000 (0.00–1.700] 4.56 [21.318]; 4.00 [1.00–1.000] 0.026 Mean intensity of spontaneous speech (dB), on-stimulation/off-medication 2.769 [2.500; [3.000] 6.761 [2.31]; 4.100 [3.00–2.400]	Maximum phonation time (MPT) (s) off-medication	15.11 [+5.13]: 14.00 {8.00-26.00}	14.73 [+5.67]: 13.85 {4.00-26.00}	0.842	
Mean intensity of sustained phonation (dB) off-medication 72.44 [27.40]; 73.00 (60.00-86.00] 73.37 [16.82]; 71.15 (63.00-89.00] 0.977 Mean intensity of sustained phonation (dB) on-medication 71.33 [16.12]; 74.00 (62.00-78.00] 72.75 [27.86]; 72.00 (59.00-87.00) 0.609 Count rate (ill/s) on-medication 4.15 [12.91, 464 [25.0-6.57] 5.08 [1.12]; 54.21 [1.50-7.75] 0.777 Perceptual severity of dysarthria (1-4) on-medication 3.88 [1.03]; 4.00 [3.00-4.00] 3.93 [1.0.25]; 4.00 [3.00-4.00] 0.162 Postoperative variable 21.67 [1.6.32]; 23.00 (6.00-29.00] 17.94 [1.4.42]; 18.50 [9.00-24.00] 0.621 UPDRS part-III on-stimulation/off-medication 3.76 [1.15.76]; 42.00 [14.00-58.00] 24.56 [1.5.03]; 13.00 (13.00-56.00] 0.611 UPDRS salinesia subscore, on-stimulation/off-medication 15.27 [1.6.63]; 10.20 (16.00-23.00] 8.81 [1.3.03]; 9.00 (2.00-14.00] 0.011 UPDRS salinesia subscore, on-stimulation/off-medication 9.78 [1.5.76]; 8.200 [1.00-25.00] 6.84 [1.4.22]; 6.5.0 [37.00-70.00] 0.612 UPDRS salinesia subscore, on-stimulation/off-medication 9.78 [1.5.69]; 59.00 [5.00-67.00] 6.84 [1.4.02]; 6.5.0 [37.00-70.00] 0.022 Mean intensity of spontaneous speech (dB), on-stimulation/off-medication 59.89 [1.4.48]; 58.00 [5.00-7.00]	Maximum phonation time (MPT) (s) on-medication	14.55 [+4.44]: 15.00 {7.00-21.00}	17.56 [+5.66]: 18.50 {7.00-26.00}	0.165	
Mean intensity of sustained phonation (dB) on-medication 123 [16.12]; 74.00 [62.00-78.00] 72.75 [17.68]; 72.00 [59.00-67.00] 6069 Count rate (sills) off-medication 4.61 [10.94]; 4.75 [3.00-5.67] 5.08 [11.47]; 4.97 [1.90-7.75] 0.370 Count rate (sills) off-medication 3.88 [10.33]; 4.00 [3.00-4.00] 3.93 [10.25]; 4.00 [3.00-4.00] 0.30 Perceptual severity of dysarthria (1-4) on-medication 3.88 [10.33]; 4.00 [3.00-4.00] 4.00 [10.00-4.00] (3.00-4.00] 0.182 Postoperative variable	Mean intensity of sustained phonation (dB) off-medication	72.44 [+7.40]: 73.00 {60.00-86.00}	73.37 [+6.82]; 71.50 {63.00-89.00}	0.977	
Count rate (all/s) of:medication4.61 [±0.94]; 4.75 [3.00–5.67]5.08 [±1.47]; 4.97 [1.90–7.75]0.380Count rate (all/s) on-medication4.73 [±1.23]; 4.64 [±5.0-6.33]4.86 [±1.62]; 4.82 [1.50–7.75]0.777Perceptul severity of dysarthria (1-4) on-medication3.88 [±0.33]; 4.00 [3.00–4.00]3.93 [±0.25]; 4.00 [3.00–4.00]0.673Perceptul severity of dysarthria (1-4) on-medication3.88 [±0.33]; 4.00 [3.00–4.00]4.00 [±0.00]; 4.00 [4.00–4.00]0.673Perceptul severity of dysarthria (1-4) on-medication3.88 [±0.33]; 4.00 [3.00–4.00]1.794 [±4.42]; 1.850 [9.00–24.00]0.023UPDRS part-III on-stimulation/of-medication21.67 [±6.32]; 23.00 [6.00–29.00]17.94 [±4.42]; 1.850 [9.00–24.00]0.023UPDRS part-III on-stimulation/of-medication27.67 [±1.576]; 42.20 [14.00–38.00]12.31 [±5.42]; 11.00 [5.00–24.00]0.011UPDRS akinesia subscore, on-stimulation/of-medication15.22 [±6.46]; 17.00 [3.00–23.00]8.81 [±3.08]; 9.00 [2.00–14.00]0.012UPDRS akinesia subscore, on-stimulation/of-medication9.78 [±5.63]; 10.00 [0.00–17.00]4.56 [±3.18]; 4.00 [1.00–10.00]0.024UPDRS akinesia subscore, on-stimulation/of-medication9.78 [±5.63]; 10.00 [5.00–67.00]64.41 [±5.74]; 63.00 [57.00–71.00]0.002Mean intensity of spontaneous speech (dB), on-stimulation/of-medication9.78 [±5.43]; 13.00 [56.00–67.00]64.81 [±4.91]; 65.00 [57.00–71.00]0.002Mean intensity of spontaneous speech (H2) on-stimulation/of-medication33.87 [±1.40]; 31.36 [±1.00–61.30]34.71 [±1.741]; 31.45 [±4.98–80.24]0.610P OS D of spontaneous speech (H2) on-stimulation/of-medic	Mean intensity of sustained phonation (dB) on-medication	71.33 [±6.12]; 74.00 {62.00-78.00}	72.75 [±7.68]; 72.00 {59.00-87.00}	0.609	
Description Description Description Description Description Count rate (sills) on -medication 3.88 [± 0.33]; 4.00 [3.00–4.00] 3.93 [± 0.25]; 4.00 [3.00–4.00] 0.873 Perceptual severity of dysarthria (1–4) onf-medication 3.88 [± 0.33]; 4.00 [3.00–4.00] 3.93 [± 0.25]; 4.00 [3.00–4.00] 0.873 Perceptual severity of dysarthria (1–4) onf-medication 3.88 [± 0.33]; 4.00 [3.00–4.00] 1.7.94 [± 4.42]; 1.8.50 [9.00–4.00] 0.023 Perceptual severity of dysarthria (1–4) onf-medication 21.67 [± 6.32]; 23.00 [6.00–29.00] 12.94 [± 4.42]; 1.8.50 [9.00–24.00] 0.024 UPDRS part-III on-stimulation/off-medication 22.00 [± 1.1.3]; 22.00 [5.00–32.00] 8.81 [± 3.08]; 9.00 [2.00–41.00] 0.011 UPDRS akinesia subscore, on-stimulation/off-medication 22.00 [± 1.1.3]; 22.00 [4.00–28.00] 15.94 [± 4.54]; 17.00 [8.00–26.00] 0.012 UPDRS akinesia subscore, off-stimulation/off-medication 20.00 [± 7.42]; 20.00 [4.00–28.00] 15.94 [± 4.54]; 17.00 [8.00–26.00] 0.013 Mean intensity of spontaneous speech (4B), on-stimulation/off-medication 59.87 [± 4.50]; 16.20 [± 5.50]; 7.07.00.0 0.013 Mean intensity of spontaneous speech (4B), on-stimulation/off-medication 35.87 [± 1.43]; 31.64 [± 2.0–7.00] 64.81 [± 4.02]; 45.51 [5 7.07.70.00]	Count rate (sill/s) off-medication	4.61 [+0.94]: 4.75 {3.00-5.67}	5.08 [+1.47]: 4.97 {1.90–7.75}	0.380	
Interstry Interstry Interstry Interstry Interstry Perceptual severity of dysarthria (1-4) off-medication 3.88 [± 0.3]; 4.00 [3.00-4.00] 3.93 [± 0.2]; 4.00 [3.00 -4.00] 0.732 Perceptual severity of dysarthria (1-4) on-medication 3.88 [± 0.3]; 4.00 [3.00-4.00] 4.00 [± 0.00]; 4.00 [4.00-4.00] 0.182 Postoperative variable UPDRS part-II off-medication 1.67 [± 6.32]; 23.00 [6.00-29.00] 1.794 [± 4.42]; 18.50 [9.00-24.00] 0.053 UPDRS part-III on-stimulation/off-medication 21.67 [± 6.32]; 23.00 [1.00-58.00] 2.455 [± 6.55]; 23.00 [1.30.0-36.00] 0.051 UPDRS akinesia subscore, on-stimulation/off-medication 22.00 [± 11.13]; 22.00 [5.00-38.00] 1.231 [± 5.42]; 11.00 [5.00-24.00] 0.011 UPDRS akinesia subscore, on-stimulation/off-medication 9.78 [± 5.63]; 10.00 [0.00-17.00] 4.56 [± 3.18]; 4.00 [1.00-10.00] 0.02 Mean intensity of spontaneous speech (dB), on-stimulation/off-medication 20.78 [± 5.09]; 59.00 [52.00-69.00] 64.81 [± 4.02]; 65.00 [57.00-70.00] 0.013 Mean intensity of spontaneous speech (Hz) on-stimulation/off-medication 35.87 [± 1.403]; 3.07 [10.12-92.55 25.98 [± 1.073]; 27.17 [7.84-42.0] 0.992 I OS D of spontaneous speech (Hz) on-stimulation/off-medication 35.87 [± 1.403]; 3.1	Count rate (sill/s) on-medication	4.73 [+1.23]: 4.64 {2.50–6.33}	4.86 [+1.62]: 4.82 {1.50-7.75}	0.777	
Brick production Brick production <thb< td=""><td>Perceptual severity of dysarthria (1–4) off-medication</td><td>3.88 [+0.33]: 4.00 {3.00-4.00}</td><td>3.93 [+0.25]; 4.00 {3.00-4.00}</td><td>0.673</td></thb<>	Perceptual severity of dysarthria (1–4) off-medication	3.88 [+0.33]: 4.00 {3.00-4.00}	3.93 [+0.25]; 4.00 {3.00-4.00}	0.673	
Destoperative variable Destoperative variable Destoperative variable UPDRS part-II off-medication 21.67 [± 6.32]; 23.00 [6.00-29.00] 17.94 [± 4.42]; 18.50 [9.00-24.00] 0.023 UPDRS part-III on-stimulation/off-medication 37.67 [± 15.76]; 42.00 [14.00-58.00] 24.56 [± 6.59]; 23.00 [13.00-26.00] 0.017 UPDRS akinesia subscore, on-stimulation/off-medication 12.20 [± 6.42]; 10.00 [3.00-23.00] 12.31 [± 5.42]; 11.00 [5.00-24.00] 0.017 UPDRS akinesia subscore, on-stimulation/off-medication 9.78 [± 5.63]; 10.00 (0.00-17.00] 4.56 [± 3.18]; 4.00 [1.00-10.00] 0.024 UPDRS akinesia subscore, on-stimulation/off-medication 9.00 [± 7.42]; 20.00 [4.00-28.00] 15.94 [± 4.54]; 17.00 [8.00-26.00] 0.005 Mean intensity of spontaneous speech (dB), on-stimulation/off-medication 59.89 [± 4.48]; 58.00 [5.60-67.00] 64.81 [± 4.02]; 65.50 [57.00-7.00] 0.013 Mean intensity of spontaneous speech (Hz) on-stimulation/off-medication 55.87 [± 14.03]; 31.66 [21.06-61.83] 34.71 [± 7.61]; 31.45 [14.98-80.24] 0.610 F0 SD of spontaneous speech (Hz) on-stimulation/off-medication 35.87 [± 4.30]; 63.00 [5.00-74.00] 63.81 [± 3.3]; 12.01 [5.00 [± 5.31]; 12.00 [± 5.00]; 57.00] 0.672 F0 SD of spontaneous speech (Hz) on-stimulation/off-medication 35.8 [± 6.23]; 10.00 [0.00	Perceptual severity of dysarthria (1–4) on-medication	3.88 [+0.33]: 4.00 {3.00-4.00}	4.00 [+0.00]: 4.00 {4.00-4.00}	0.182	
UPDRS part-II off-medication 2167 [±6.32]; 23.00 [6.00-29.00] 17.94 [±4.42]; 18.50 [9.00-24.00] 0.023 UPDRS part-III on-stimulation/off-medication 37.67 [±15.76]; 42.00 [14.00-58.00] 24.56 [±6.95]; 23.00 [13.00-36.00] 0.017 UPDRS part-III on-stimulation/off-medication 22.00 [±11.13]; 22.00 [5.00-38.00] 12.31 [±5.42]; 11.00 [5.00-24.00] 0.017 UPDRS akinesia subscore, on-stimulation/off-medication 97.8 [±5.63]; 10.00 [0.00-17.00] 4.56 [±3.18]; 4.00 [10.00-10.00] 0.024 UPDRS akinesia subscore, on-stimulation/off-medication 97.8 [±5.63]; 10.00 [0.00-17.00] 4.56 [±3.18]; 4.00 [15.00-10.00] 0.024 UPDRS akinesia subscore, off-stimulation/off-medication 97.8 [±5.09]; 59.00 [52.00-69.00] 64.81 [±4.54]; 17.00 [8.00-26.00] 0.024 Mean intensity of spontaneous speech (BJ), on-stimulation/off-medication 59.89 [±4.48]; 58.00 [56.00-67.00] 64.81 [±4.02]; 65.50 [57.00-70.00] 0.038 F0 SD of spontaneous speech (Hz) on-stimulation/off-medication 35.77 [±1.403]; 31.69 [1.00-72.80] 52.98 [±0.75]; 7.17 (78.44.42.0] 0.019 F0 SD of spontaneous speech (Hz) on-stimulation/off-medication 33.51 [±2.28]; 10.00 [7.00-25.00] 16.38 [±7.33]; 15.00 (62.0-32.00] 0.173 Maximum phonation time (MPT) (s) on-stimulation/off-medication 33.51 [±2	Postoperative variable				
DescriptionDescriptionDescriptionDescriptionDescriptionDescriptionUPDRS part-III on-stimulation/off-medication $2.200 [\pm 11.13]; 22.00 [5.00-38.00]$ $21.31 [\pm 5.42]; 11.00 [5.00-24.00]$ 0.017UPDRS akinesia subscore, on-stimulation/off-medication $5.22 [\pm 6.46]; 17.00 [3.00-23.00]$ $8.81 [\pm 3.08]; 9.00 (2.00-14.00)$ 0.011UPDRS akinesia subscore, on-stimulation/off-medication $9.78 [\pm 5.63]; 10.00 (0.00-17.00]$ $4.56 [\pm 3.18]; 4.00 (1.00-10.00]$ 0.024UPDRS akinesia subscore, on-stimulation/off-medication $9.78 [\pm 5.63]; 10.00 (0.00-17.00]$ $4.56 [\pm 3.18]; 4.00 (1.50-0.00]$ 0.062Mean intensity of spontaneous speech (dB), on-stimulation/off-medication $9.78 [\pm 5.09]; 59.00 (52.00-69.00]$ $6.84 [\pm 5.74]; 68.00 (57.00-78.00]$ 0.013Mean intensity of spontaneous speech (dB), on-stimulation/off-medication $59.89 [\pm 4.48]; 58.00 (56.00-67.00]$ $6.81 [\pm 3.02]; 65.50 (57.00-77.00]$ 0.013Mean intensity of spontaneous speech (H2) on-stimulation/off-medication $37.24 [\pm 2.3.43]; 3.07 (10.2-92.56]$ $25.98 [\pm 10.75]; 27.17 (7.84-44.20]$ 0.193F0 SD of spontaneous speech (H2) on-stimulation/off-medication $37.24 [\pm 2.3.43]; 3.07 (10.2-92.56]$ $25.88 [\pm 1.75]; 15.20 (5.60-76.00]$ 0.13Maximum phonation time (MPT) (s) on-stimulation/off-medication $37.24 [\pm 2.3.43]; 3.09 (10.2-92.56]$ $13.87 [\pm 5.73]; 15.00 (5.00-78.00]$ 0.13Maximum phonation time (MPT) (s) on-stimulation/off-medication $37.24 [\pm 2.3.43]; 3.09 (10.2-92.56]$ $13.87 [\pm 3.51]; 13.05 (12.0-97.00]$ 0.163Maximum phonation time (MPT) (s) on-stimulation/off-medication $37.24 $	UPDRS part-II off-medication	21.67 [+6.32]: 23.00 {6.00-29.00}	17.94 [+4.42]: 18.50 {9.00-24.00}	0.023	
Display and manufaction Display functions during Display functions Display functions <thdisplay functions<="" th=""> <thdisplay functions<="" td=""><td>UPDRS part-III on-stimulation/off-medication</td><td>37 67 [+15 76]: 42 00 {14 00-58 00}</td><td>24 56 [+6 95]: 23 00 {13 00-36 00}</td><td>0.054</td></thdisplay></thdisplay>	UPDRS part-III on-stimulation/off-medication	37 67 [+15 76]: 42 00 {14 00-58 00}	24 56 [+6 95]: 23 00 {13 00-36 00}	0.054	
Def per from part instruction interaction 1522 [4:46]; 17.00 [3.00-23.00]8.81 [4:36]; 300 [2:00-14:00]0.011UPDRS akinesia subscore, on-stimulation/off-medication 978 [±5.63]; 10.00 (0.00-17.00] 4.56 [±3.18]; 4.00 [1:00-10.00]0.024UPDRS akinesia subscore, off-stimulation/off-medication 2000 [±7.42]; 20.00 [4:00-28.00] 15.94 [±4.54]; 17.00 [8:00-26.00]0.065Mean intensity of spontaneous speech (dB), on-stimulation/off-medication 59.78 [±5.09]; 59.00 [52.00-69.00] 68.44 [±5.74]; 68.00 (57.00-81.00]0.002Mean intensity of spontaneous speech (dB), on-stimulation/off-medication 59.87 [±4.81]; 86.00 [56.00-67.00] 67.87 [±4.50]; 68.50 [57.00-70.00]0.013Mean intensity of spontaneous speech (dB), on-stimulation/off-medication 35.87 [±1.403]; 31.66 [21.06-61.83] 34.71 [±17.61]; 31.45 [14.98-80.24]0.010F0 SD of spontaneous speech (Hz) on-stimulation/off-medication 35.87 [±1.30]; 10.12-92.56] 25.98 [±1.075]; 27.17 (7.84-44.20]0.193F0 SD of spontaneous speech (Hz) on-stimulation/off-medication 39.88 [±1.33]; 31.92 [25.85-63.47] 29.26 [±11.32]; 28.15 [13.87-46.79]0.079Maximum phonation time (MPT) (s) on-stimulation/off-medication 33.57 [±6.28]; 11.00 (7.00-25.00]163.8 [±7.33]; 15.00 [62.0-32.00]0.014Maximum phonation time (MPT) (s) on-stimulation/off-medication 3.85 [±6.28]; 11.00 (7.00-17.00]14.84 [±6.30]; 14.50 (5.00-88.00]0.020Maximum phonation time (MPT) (s) on-stimulation/off-medication 3.57 [±6.28]; 11.00 (7.00-17.00]14.84 [±6.30]; 14.50 (5.00-88.00]0.021Maximum phonation time (MPT) (s) on-stimulation/	UPDRS part-III on-stimulation/on-medication	22.00 [+11.13]: 22.00 {5.00-38.00}	$12, 31 [+5, 42]; 11, 00 \{5, 00-24, 00\}$	0.017	
Non-Less dataNon-Less dataNon-Less dataNon-Less dataNon-Less dataUPDRS akinesia subscore, on-stimulation/on-medication $9.78 [\pm 5.3]; 10.00 (0.00-17.00]$ $4.56 [\pm 3.18]; 4.00 (1.00-01.000]$ 0.062 UPDRS akinesia subscore, off-stimulation/off-medication $20.00 [\pm 7.42]; 20.00 (4.00-28.00]$ $15.94 [\pm 4.54]; 17.00 [8.00-26.00]$ 0.062 Mean intensity of spontaneous speech (dB), on-stimulation/off-medication $59.78 [\pm 5.09]; 59.00 (52.00-69.00]$ $64.81 [\pm 4.02]; 65.50 [57.00-70.00]$ 0.013 Mean intensity of spontaneous speech (H2) on-stimulation/off-medication $66.7 [\pm 5.77]; 58.00 (54.00-70.00]$ $67.87 [\pm 4.50]; 68.50 (55.00-74.00]$ 0.008 F0 SD of spontaneous speech (H2) on-stimulation/off-medication $35.87 [\pm 14.03]; 31.66 (21.06-61.83)$ $34.71 [\pm 7.61]; 31.45 [14.98-80.24]$ 0.610 F0 SD of spontaneous speech (H2) on-stimulation/off-medication $39.08 [\pm 13.33]; 31.97 [10.12-92.56]$ $25.98 [\pm 10.75]; 27.17 (7.84-44.20)$ 0.978 F0 SD of spontaneous speech (H2) on-stimulation/off-medication $39.08 [\pm 13.33]; 31.92 [25.85-63.47]$ $29.26 [\pm 11.32]; 28.15 [33.87-46.79]$ 0.079 Maximum phonation time (MPT) (s) on-stimulation/off-medication $38.5 [\pm 4.34]; 9.00 [5.00-18.00]$ $13.67 [\pm 5.31]; 15.05 (6.20-32.00]$ 0.614 Maximum phonation time (MPT) (s) on-stimulation/off-medication $3.02 [\pm 7.41]; 64.00 [52.07-76.00]$ $12.6 [\pm 3.81]; 7.10 [4.60.97.00-25.00]$ $13.67 [\pm 5.81]; 10.5 (6.00-88.00]$ 0.020 Mean intensity of sustained phonation (dB), on-stimulation/off-medication $5.55 [\pm 10.28]; 7.100 [46.00-75.00]$ $71.31 [\pm 7.58]; 7.050 [60.00-88.00]$ $0.$	UPDRS akinesia subscore, on-stimulation/off-medication	$15 22 [+6 46]: 17 00 \{3 00-23 00\}$	8 81 [+3 08]: 9 00 {2 00-14 00}	0.011	
Note intensity of submitted protocols of the set of th	UPDRS akinesia subscore, on stimulation/on-medication	9 78 [+ 5 63]: 10 00 {0 00-17 00}	4 56 [+ 3 18]: 4 00 {1 00-10 00}	0.024	
Note interimination of the interiminatio of	UPDRS akinesia subscore, off-stimulation/off-medication	$20.00 [+7.42]: 20.00 \{4.00-28.00\}$	$15.94 [+4.54]: 17.00 \{8.00-26.00\}$	0.065	
Maximum Ny synameters presen (ab), on stimulation of medication 59.89 [±4.48]; 58.00 [56.00-67.00] 64.81 [±4.02]; 65.50 [57.00-70.00] 0.013 Mean intensity of spontaneous speech (dB), on-stimulation/off-medication 59.89 [±4.48]; 58.00 [56.00-67.00] 64.81 [±4.02]; 65.50 [57.00-70.00] 0.008 F0 SD of spontaneous speech (HZ) on-stimulation/off-medication 35.87 [±1.403]; 31.66 [21.00-61.83] 34.71 [±1.761]; 31.45 [14.98-80.24] 0.610 F0 SD of spontaneous speech (HZ) on-stimulation/off-medication 37.24 [±23.43]; 30.79 [10.12-92.56] 25.98 [±1.075]; 27.17 (7.84-44.20] 0.979 Maximum phonation time (MPT) (s) on-stimulation/off-medication 33.05 [±6.28]; 11.00 [7.00-25.00] 16.38 [±7.33]; 15.00 [6.20-32.00] 0.173 Maximum phonation time (MPT) (s) on-stimulation/off-medication 9.85 [±4.34]; 9.00 [5.00-18.00] 13.67 [±5.11]; 12.50 [8.60-27.00] 0.064 Maximum phonation time (MPT) (s) on-stimulation/off-medication 11.77 [±2.90]; 12.00 [7.00-18.00] 14.84 [±6.30]; 14.50 [7.00-31.00] 0.173 Mean intensity of sustained phonation (dB), on-stimulation/off-medication 63.02 [±7.31]; 64.00 [52.00-76.00] 72.06 [±8.38]; 71.50 [60.00-88.00] 0.021 Mean intensity of sustained phonation (dB), on-stimulation/off-medication 65.55 [±10.28]; 71.00 [46.00-75.00] 71.31 [±7.58]; 70.50 [60.00-88.00] 0.	Mean intensity of spontaneous speech (dB) on-stimulation/off-medication	59 78 [+ 5 09]: 59 00 {52 00-69 00}	68 44 [+5 74]; 68 00 {57 00-81 00}	0.002	
Natural Methyl of polation of the intervention of the interventing of the intervent	Mean intensity of spontaneous speech (dB), off-stimulation/off-medication	59 89 [+4 48]: 58 00 {56 00-67 00}	64 81 [+4 02]: 65 50 {57 00-70 00}	0.013	
Name The second spectra (us) of stimulation of medication35.87 [±14.03]; 31.66 [21.06–61.83]34.71 [±17.61]; 31.45 [14.98–80.24]0.610F0 SD of spontaneous speech (Hz) on-stimulation/off-medication37.24 [±23.43]; 30.79 [10.12–92.56]25.98 [±10.75]; 27.17 (7.84–44.20)0.193F0 SD of spontaneous speech (Hz) on-stimulation/off-medication39.08 [±13.33]; 31.92 [25.85–63.47]29.26 [±11.32]; 28.15 [13.87–46.79]0.079Maximum phonation time (MPT) (s) on-stimulation/off-medication13.35 [±6.28]; 11.00 (7.00–25.00]16.38 [±7.33]; 15.00 (6.20–32.00]0.064Maximum phonation time (MPT) (s) off-stimulation/off-medication9.85 [±4.34]; 9.00 (5.00–18.00]13.67 [±5.11]; 12.50 (8.60–27.00]0.064Maximum phonation time (MPT) (s) on-stimulation/off-medication63.00 [±7.81]; 64.00 (52.00–76.00]72.06 [±8.38]; 71.50 (56.00–88.00]0.020Mean intensity of sustained phonation (dB), on-stimulation/off-medication63.02 [±6.44]; 63.00 (55.00–74.00]69.72 [±6.71]; 68.50 (60.00–85.00]0.364Count rate (sill/s) on-stimulation/off-medication65.55 [±10.28]; 71.00 [46.00–75.00]71.31 [±7.58]; 70.50 (60.00–88.00]0.364Count rate (sill/s) on-stimulation/off-medication65.25 [±10.28]; 74.00 [45.00–75.00]71.31 [±7.58]; 70.50 (60.00–88.00]0.379Count rate (sill/s) on-stimulation/off-medication52.55 [±12.28]; 74.00 [46.00–75.00]71.31 [±7.58]; 70.50 (60.00–88.00]0.364Count rate (sill/s) on-stimulation/off-medication52.55 [±2.23]; 4.64 (2.22–7.28]41.6 [±1.22]; 4.00 [2.68–6.60]0.798Count rate (sill/s) on-stimulation/off-medication52.55 [±2.35]; 4.64 (2.32–9.44] <t< td=""><td>Mean intensity of spontaneous speech (dB), on -stimulation/on-medication</td><td>60 67 [+ 5 77]: 58 00 {54 00-70 00}</td><td>67 87 [+4 50]; 68 50 {55 00-74 00}</td><td>0.008</td></t<>	Mean intensity of spontaneous speech (dB), on -stimulation/on-medication	60 67 [+ 5 77]: 58 00 {54 00-70 00}	67 87 [+4 50]; 68 50 {55 00-74 00}	0.008	
For SD of point relation of the formation of the formatio	F0 SD of spontaneous speech (Hz) on-stimulation/off-medication	35 87 [+14 03]: 31 66 {21 06-61 83}	34 71 [+17 61]: 31 45 {14 98-80 24}	0.610	
For Stor of pointaneous speech (Hz) on stimulation on medicationStor (=2007) (1012 94.00)Stor (=2007) (1012 94.00)Stor (=2007) (1012 94.00)For SD of spontaneous speech (Hz) on-stimulation/on-medication39.08 (± 13.33); 31.92 (25.85-63.47)29.26 (± 11.32); 28.15 (13.87-46.79)0.079Maximum phonation time (MPT) (s) on-stimulation/off-medication13.35 (± 6.28); 11.00 (7.00-25.00)16.38 (± 7.33); 15.00 (6.20-32.00)0.164Maximum phonation time (MPT) (s) on-stimulation/off-medication9.85 (± 4.34); 9.00 (5.00-18.00)13.67 (± 5.11); 12.50 (8.60-27.00)0.064Maximum phonation time (MPT) (s) on-stimulation/off-medication11.77 (± 2.90); 12.00 (7.00-18.00)14.84 (± 6.30); 14.50 (7.00-31.00)0.156Mean intensity of sustained phonation (dB), on-stimulation/off-medication63.00 (± 7.81); 64.00 (52.00-76.00)72.06 (± 8.38); 71.50 (60.00-88.00)0.020Mean intensity of sustained phonation (dB), on-stimulation/off-medication63.22 (± 6.44); 63.00 (55.00-74.00)69.72 (± 6.71); 68.50 (60.00-88.00)0.031Mean intensity of sustained phonation (dB), on-stimulation/on-medication65.55 (± 10.28); 71.00 (46.00-75.00)71.31 (± 7.58); 70.50 (60.00-88.00)0.364Count rate (sill/s) on-stimulation/off-medication4.49 (± 1.80); 4.64 (2.22-7.28)4.16 (± 1.22); 4.00 (2.68-6.60)0.977Count rate (sill/s) on-stimulation/on-medication5.25 (± 2.35); 4.64 (2.32-9.44)4.64 (± 1.14); 4.44 (2.22-7.28)0.691Speech intelligibility (%), on-stimulation/off-medication73.78 (± 7.46); 78.00 (48.00-94.00)98.37 (± 2.45); 100.00 (92.00-100.00)0.000Speech intelligibility (%), on-stimulation/of	F0 SD of spontaneous speech (Hz) off-stimulation/off-medication	37 24 [+ 23 43]: 30 79 {10 12-92 56}	25 98 [+10 75]; 27 17 {7 84-44 20}	0 193	
Naximum phonation time (MPT) (s) on-stimulation/off-medication 13.35 [±6.28]; 11.00 {7.00-25.00} 16.38 [±7.33]; 15.00 {6.20-32.00} 0.173 Maximum phonation time (MPT) (s) off-stimulation/off-medication 9.85 [±4.34]; 9.00 {5.00-18.00} 13.67 [±5.11]; 12.50 {8.60-27.00} 0.064 Maximum phonation time (MPT) (s) on-stimulation/onf-medication 11.77 [±2.90]; 12.00 {7.00-18.00} 14.84 [±6.30]; 14.50 {7.00-31.00} 0.156 Mean intensity of sustained phonation (dB), on-stimulation/off-medication 63.00 [±7.81]; 64.00 {52.00-76.00} 72.06 [±8.38]; 71.50 {56.00-88.00} 0.020 Mean intensity of sustained phonation (dB), on-stimulation/off-medication 63.22 [±6.44]; 63.00 {55.00-74.00} 69.72 [±6.71]; 68.50 {60.00-85.00} 0.364 Count rate (sill/s) on-stimulation/off-medication 65.55 [±10.28]; 71.00 {46.00-75.00} 71.31 [±7.58]; 70.50 {60.00-88.00} 0.364 Count rate (sill/s) on-stimulation/off-medication 4.49 [±1.80]; 4.64 {2.22-7.28} 4.16 [±1.22]; 4.00 {2.68-6.60} 0.977 Count rate (sill/s) on-stimulation/off-medication 5.25 [±2.35]; 4.64 {2.32-9.44} 4.64 [±1.14]; 4.44 {2.22-7.28} 0.691 Speech intelligibility (%), on-stimulation/off-medication 73.78 [±17.46]; 78.00 {48.00-94.00} 98.37 [±2.45]; 100.00 {92.00-100.00} 0.000 Speech intelligibility (%), on	F0 SD of spontaneous speech (Hz) on stimulation/on-medication	39.08 [+13.33]: 31.92 {25.85-63.47}	29 26 [+11 32]: 28 15 {13 87-46 79}	0.079	
Maximum phonation time (MPT) (s) off-stimulation/off-medication Pass [=0.205], 11.00 (10.0 = 20.00] Pass [=0.205], 11.00 (10.00] Pass [=0.205], 11.00 (10.0]	Maximum phonation time (MPT) (s) on-stimulation/off-medication	$13.35[+6.28] \cdot 11.00 \{7.00-25.00\}$	$16.38[+7.33] \cdot 15.00 \{6.20-32.00\}$	0.173	
Maximum phonation time (MPT) (s) on-stimulation/on-medication 5.05 [1:1.24], 5.05 [2:0.07] 15.05 [1:1.21], 12.05 [2:0.07] 15.05 [1:1.21], 12.05 [2:0.07] 0.050 Maximum phonation time (MPT) (s) on-stimulation/on-medication 11.77 [1:2.90]; 12.00 {7.00-18.00} 14.84 [±6.30]; 14.50 {7.00-31.00} 0.156 Mean intensity of sustained phonation (dB), on-stimulation/off-medication 63.00 [±7.81]; 64.00 {52.00-76.00} 72.06 [±8.38]; 71.50 {56.00-88.00} 0.020 Mean intensity of sustained phonation (dB), on-stimulation/off-medication 63.22 [±6.44]; 63.00 {55.00-74.00} 69.72 [±6.71]; 68.50 {60.00-85.00} 0.314 Mean intensity of sustained phonation (dB), on-stimulation/on-medication 65.55 [±10.28]; 71.00 {46.00-75.00} 71.31 [±7.58]; 70.50 {60.00-88.00} 0.364 Count rate (sill/s) on-stimulation/off-medication 4.49 [±1.80]; 4.64 {2.22-7.28} 4.16 [±1.22]; 4.00 {2.68-6.60} 0.798 Count rate (sill/s) on-stimulation/off-medication 4.15 [±1.47]; 4.25 {1.46-6.37} 4.16 [±0.99]; 4.44 {2.55-5.66} 0.977 Count rate (sill/s) on-stimulation/off-medication 5.25 [±2.35]; 4.64 {2.32-9.44} 4.64 [±1.14]; 4.44 {2.22-7.28} 0.691 Speech intelligibility (%), on-stimulation/off-medication 7.378 [±17.46]; 78.00 {48.00-94.00} 98.37 [±2.45]; 100.00 {92.00-100.00} 0.000 Speech intelligibility (%), on-stimulation/on-medica	Maximum phonation time (MPT) (s) off-stimulation/off-medication	9.85 [+4.34] 9.00 {5.00_18.00}	13.67 [+5.11]: 12.50 {8.60_27.00}	0.064	
Maximum prioritation time (M1 7) (5) on stimulation on medication 11.77 [22.50], 12.50 (7.50-71.50] 14.47 [21.50], 14.50 (7.50-71.50] 61.75 Mean intensity of sustained phonation (dB), on-stimulation/off-medication 63.00 [+7.81]; 64.00 {52.00-76.00} 72.06 [±8.38]; 71.50 {56.00-88.00} 0.020 Mean intensity of sustained phonation (dB), on-stimulation/off-medication 63.22 [±6.44]; 63.00 {55.00-74.00} 69.72 [±6.71]; 68.50 {60.00-85.00} 0.031 Mean intensity of sustained phonation (dB), on-stimulation/on-medication 65.55 [±10.28]; 71.00 {46.00-75.00} 71.31 [±7.58]; 70.50 {60.00-88.00} 0.364 Count rate (sill/s) on-stimulation/off-medication 4.49 [±1.80]; 4.64 {2.22-7.28} 4.16 [±1.22]; 4.00 {2.68-6.60} 0.798 Count rate (sill/s) on-stimulation/off-medication 4.15 [±1.47]; 4.25 {1.46-6.37} 4.16 [±0.99]; 4.44 {2.52-5.66} 0.977 Count rate (sill/s) on-stimulation/off-medication 5.25 [±2.35]; 4.64 {2.32-9.44} 4.64 [±1.14]; 4.44 {2.22-7.28} 0.691 Speech intelligibility (%), on-stimulation/off-medication 73.78 [±17.46]; 78.00 {48.00-94.00} 98.37 [±2.45]; 100.00 {92.00-100.00} 0.000 Speech intelligibility (%), on-stimulation/off-medication 66.78 [±18.71]; 64.00 {48.00-94.00} 94.22 [±6.52]; 96.00 {78.00-100.00} 0.001 Speech intelligibility (%), on-stimulation/on-medication 69.56 [±22.53];	Maximum phonation time (MPT) (s) on-stimulation/on-medication	$11.77[+2.90] \cdot 12.00 \{7.00-18.00\}$	$14.84 [+6.30] \cdot 14.50 \{7.00-31.00\}$	0.004	
Mean intensity of sustained phonation (db), off-stimulation/off-medication 63.22 [±6.31], 94.00 [52.00-76.00] 72.00 [10.50], 71.50 [50.00-50.00] 0.031 Mean intensity of sustained phonation (dB), off-stimulation/off-medication 63.22 [±6.44]; 63.00 {55.00-74.00} 69.72 [±6.71]; 68.50 {60.00-88.00} 0.031 Mean intensity of sustained phonation (dB), on-stimulation/on-medication 65.55 [±10.28]; 71.00 {46.00-75.00} 71.31 [±7.58]; 70.50 {60.00-88.00} 0.364 Count rate (sill/s) on-stimulation/off-medication 4.49 [±1.80]; 4.64 {2.22-7.28} 4.16 [±1.22]; 4.00 {2.68-6.60} 0.798 Count rate (sill/s) on-stimulation/off-medication 4.15 [±1.47]; 4.25 {1.46-6.37} 4.16 [±0.99]; 4.44 {2.55-5.66} 0.977 Count rate (sill/s) on-stimulation/off-medication 5.25 [±2.35]; 4.64 {2.32-9.44} 4.64 [±1.14]; 4.44 {2.22-7.28} 0.691 Speech intelligibility (%), on-stimulation/off-medication 73.78 [±17.46]; 78.00 {48.00-94.00} 98.37 [±2.45]; 100.00 {92.00-100.00} 0.000 Speech intelligibility (%), on-stimulation/off-medication 66.78 [±18.71]; 64.00 {48.00-94.00} 94.22 [±6.52]; 96.00 {76.00-100.00} 0.001 Speech intelligibility (%), on-stimulation/on-medication 69.56 [±22.53]; 80.00 {28.00-92.00} 93.12 [±7.59]; 96.00 {76.00-100.00} 0.001	Mean intensity of sustained phonation (dB) on-stimulation/off-medication	$(\pm 2.50], 12.00, (500-10.00)$	72.06 [+8.38], 71.50 [56.00_88.00]	0.130	
Mean intensity of sustained phonation (ab), on-stimulation/on-medication 65.52 [±0.74], 65.00 [55.00-74.00] 65.72 [±0.74], 65.00 [65.00-75.00] 67.72 [±0.74], 65.00 [65.00-75.00] Mean intensity of sustained phonation (dB), on-stimulation/on-medication 65.55 [±10.28]; 71.00 [46.00-75.00] 71.31 [±7.58]; 70.50 [60.00-88.00] 0.364 Count rate (sill/s) on-stimulation/off-medication 4.49 [±1.80]; 4.64 [2.22-7.28] 4.16 [±1.22]; 4.00 [2.68-6.60] 0.798 Count rate (sill/s) off-stimulation/off-medication 4.15 [±1.47]; 4.25 [1.46-6.37] 4.16 [±0.99]; 4.44 [2.55-5.66] 0.977 Count rate (sill/s) on-stimulation/off-medication 5.25 [±2.35]; 4.64 [2.32-9.44] 4.64 [±1.14]; 4.44 [2.22-7.28] 0.691 Speech intelligibility (%), on-stimulation/off-medication 5.25 [±2.35]; 4.64 [2.32-9.44] 9.837 [±2.45]; 100.00 [92.00-100.00] 0.000 Speech intelligibility (%), on-stimulation/off-medication 66.78 [±18.71]; 64.00 [48.00-94.00] 94.22 [±6.52]; 96.00 [78.00-100.00] 0.000 Speech intelligibility (%), on-stimulation/on-medication 69.56 [±22.53]; 80.00 [28.00-92.00] 93.12 [±7.59]; 96.00 [76.00-100.00] 0.001	Mean intensity of sustained phonation (dB), off-stimulation/off-medication	$(52.00 [\pm 7.01], 04.00 [52.00 - 70.00]$	69 72 [+ 6 71]: 68 50 [60 00_85 00]	0.020	
Count rate (sill/s) on-stimulation/off-medication 6.3.5 [±10.26], 71.50 [40.00-73.03] 71.51 [±1.35], 70.30 (40.00-83.03] 60.304 Count rate (sill/s) on-stimulation/off-medication 4.49 [±1.80]; 4.64 {2.22-7.28} 4.16 [±1.22]; 4.00 {2.68-6.60} 0.798 Count rate (sill/s) off-stimulation/off-medication 4.15 [±1.47]; 4.25 {1.46-6.37} 4.16 [±0.99]; 4.44 {2.25-5.66} 0.977 Count rate (sill/s) on-stimulation/off-medication 5.25 [±2.35]; 4.64 {2.32-9.44} 4.64 [±1.14]; 4.44 {2.22-7.28} 0.691 Speech intelligibility (%), on-stimulation/off-medication 66.78 [±18.71]; 64.00 {48.00-94.00} 98.37 [±2.45]; 100.00 {92.00-100.00} 0.000 Speech intelligibility (%), on-stimulation/on-medication 69.56 [±22.53]; 80.00 {28.00-92.00} 93.12 [±7.59]; 96.00 {76.00-100.00} 0.001	Mean intensity of sustained phonation (dB) , on stimulation/on-medication	$65.55 [\pm 10.28], 71.00 [46.00, 75.00]$	71 31 [+7 58]; 70 50 [60:00 88 00]	0.051	
Count rate (sin/s) of stimulation/off-medication 4.15 [±1.00], 4.04 [2.22-7.26] 4.16 [±1.22] 4.00 [2.06-0.00] 0.798 Count rate (sill/s) off-stimulation/off-medication 4.15 [±1.47]; 4.25 {1.46-6.37} 4.16 [±0.99]; 4.44 {2.55-5.66} 0.977 Count rate (sill/s) on-stimulation/off-medication 5.25 [±2.35]; 4.64 {2.32-9.44} 4.64 [±1.14]; 4.44 {2.22-7.28} 0.691 Speech intelligibility (%), on-stimulation/off-medication 73.78 [±17.46]; 78.00 {48.00-94.00} 98.37 [±2.45]; 100.00 {92.00-100.00} 0.000 Speech intelligibility (%), on-stimulation/off-medication 66.78 [±18.71]; 64.00 {48.00-94.00} 94.22 [±6.52]; 96.00 {78.00-100.00} 0.000 Speech intelligibility (%), on-stimulation/on-medication 69.56 [±22.53]; 80.00 {28.00-92.00} 93.12 [±7.59]; 96.00 {76.00-100.00} 0.001	Count rate (sill/s) on-stimulation/off-medication	$4 49 [+1 80] \cdot 4 64 \{2 22 - 7 28\}$	4 16 [+1 22]· 4 00 ½ 68_6 60	0.798	
Count rate (sind) of similation of medication 4.15 [1:47], 4.25 [1:40-0.37] 4.16 [1:0.37], 4.44 [2:35-3:06] 0.977 Count rate (sills) on-stimulation/on-medication 5.25 [±2.35]; 4.64 [2:32-9.44] 4.64 [±1.14]; 4.44 [2:22-7.28] 0.691 Speech intelligibility (%), on-stimulation/off-medication 73.78 [±17.46]; 78.00 [48.00-94.00] 98.37 [±2.45]; 100.00 [92.00-100.00] 0.000 Speech intelligibility (%), on-stimulation/off-medication 66.78 [±18.71]; 64.00 [48.00-94.00] 94.22 [±6.52]; 96.00 [78.00-100.00] 0.000 Speech intelligibility (%), on-stimulation/on-medication 69.56 [±22.53]; 80.00 [28.00-92.00] 93.12 [±7.59]; 96.00 [76.00-100.00] 0.001	Count rate (sill/s) off-stimulation/off-medication	$4 15 [+1.47] \cdot 4 25 11.46 - 6.371$	4 16 [+0.99] 4 44 \$2.55 - 5.66	0.977	
Speech intelligibility (%), on-stimulation/off-medication 5.25 [± 2.53], 4.04 [2.52-7.44] 4.04 [± 1.14]; 4.44 [2.22-7.26] 0.091 Speech intelligibility (%), on-stimulation/off-medication 73.78 [± 17.46]; 78.00 [48.00-94.00] 98.37 [± 2.45]; 100.00 [92.00-100.00] 0.000 Speech intelligibility (%), on-stimulation/off-medication 66.78 [± 18.71]; 64.00 [48.00-94.00] 94.22 [± 6.52]; 96.00 [78.00-100.00] 0.000 Speech intelligibility (%), on-stimulation/on-medication 69.56 [± 22.53]; 80.00 [28.00-92.00] 93.12 [± 7.59]; 96.00 [76.00-100.00] 0.001	Count rate (sill/s) on-stimulation/on-incutcation	$5.25 [+ 2.35] \cdot 4.64 52.22 \cdot 0.44$	$4.64 [+1.14] \cdot 4.44 (2.22) = 7.20 [-0.22]$	0.601	
Speech intelligibility (%), on-stimulation/on-medication 65.7 [±17.40] / 8.00 [48.00-94.00] 96.7 [±2.45]; 100.00 [22.00-100.00] 0.000 Speech intelligibility (%), on-stimulation/on-medication 66.78 [±18.71]; 64.00 [48.00-94.00] 94.22 [±6.52]; 96.00 [78.00-100.00] 0.000 Speech intelligibility (%), on-stimulation/on-medication 69.56 [±22.53]; 80.00 [28.00-92.00] 93.12 [±7.59]; 96.00 [76.00-100.00] 0.001	Speech intelligibility (%) on stimulation/off modication	73 78 [+ 17 46], 78 00 /48 00 04 00]	1.14, 1.14 , 1.14 , 1.14 , 2.22 , 2.0	0.091	
Speech intelligibility (%), on-stimulation/on-medication 69.56 [±22.53]; 80.00 {28.00-92.00} 93.12 [±7.59]; 96.00 {76.00-100.00} 0.001	Speech intelligibility (%) off stimulation/off modication	66 78 [+ 18 71]; 64 00 [48 00 04 00]	94 22 [+6 52], 96 00 /78 00 100 00]	0.000	
speech intengroundy (70), 011-summation/011-intendention [05.00 [±22.55]; 00.00 {20.00-92.00} [53.12 [±7.59]; 90.00 {(0.00-100.00] [0.001]	Speech intelligibility (%) on stimulation/on-medication	60.56 [± 20.71], 04.00 [40.00-94.00]	93 12 [+ 7 50], 96 00 [76 00 100 00]	0.000	
Continued	Continued	09.50 [± 22.55], 00.00 [20.00-92.00]	23.12 [± 7.32], 20.00 {70.00-100.00}	0.001	

	No. (%); Mean [±SD]; median {range}			
Variable	"Worsened" (n=9)	"Stable/improved" (n = 16)	P value	
Perceptual severity of dysarthria (1-4) on-stimulation/off-medication	2.88 [±0.78]; 3.00 {1.00-4.00}	3.68 [±0.47]; 4.00 {3.00-4.00}	0.005	
Perceptual severity of dysarthria (1-4) off-stimulation/off-medication	2.88 [±0.78]; 3.00 {2.00-4.00}	3.67 [±0.49]; 4.00 {3.00-4.00}	0.010	
Perceptual severity of dysarthria (1-4) on-stimulation/on-medication	3.00 [±0.86]; 3.00 {2.00-4.00}	3.43 [±0.51]; 3.00 {3.00-4.00}	0.191	
Trail making test part B	242.71 [±146.45]; 232.00 {74.00-531.00}	116.80 [±95.23]; 97.50 {27.00-310.00}	0.05	

Table 3. Differences in clinical and speech variables between "worsened" and "stable" subgroups. *PD* Parkinson disease, *LEDD* Levodopa Equivalent Daily Dose, *PIGD* dominant postural instability and gait disorder, *SD* standard deviation, *UPDRS* Unified Parkinson's Disease Rating Scale.

study that underlined the potential predictor role of preoperative cognitive function for speech deterioration after STN-DBS¹⁹. The trend toward the significance of PIGD subscores between the two "worsened" and "stable" subgroups suggests a possible link between speech deterioration and axial features, confirming the correlation between hypokinetic dysarthria and PD axial symptoms⁸. A similar tendency towards significance was also found for the over-distribution of GBA1-PD patients in the "worsened" group. GBA1-PD patients complain about higher axial and cognitive burden when compared with wild-type PD patients²⁰ leading to the assumption that GBA1-PD patients may be at higher risk of developing post-operatively not only gait and cognitive worsening but also speech deterioration. Interestingly, disease duration, sex, duration of follow-up and the total electrical energy delivered by STN-DBS²¹ did not significantly differ between the two groups. This result is in line with a previous study that did not find any association between speech intelligibility deterioration and disease duration⁷ even if another study by Tripoliti et al.⁹ found that disease duration was a predictive factor for speech outcome. In addition, concerning preoperative speech variables we did not find differences between the two groups, while postoperatively, both speech intelligibility and mean intensity of spontaneous speech were significantly lower in the worsened group if compared with the stable one. With regards to the comparison between the different speech variables, a statistically significant reduction of the intensity of sustained phonation emerged in the offstimulation/off-medication condition if compared with the on-stimulation/off-medication condition highlighting the possible positive effect of STN-DBS on voice intensity, as already confirmed in previous studies 7.18. The improvement of speech intensity due to STN-DBS has been linked to its effects on hypokinesia and rigidity of language-related organs^{18,22} which represent one of the major pathophysiological bases of hypokinetic dysarthria, characterized by hypophonia, monotony, hypoarticulation of consonants and inappropriate silences²³.

A further result that emerged in our sample was the significant reduction of the maximum phonation time (MPT) in the off-stimulation/off-medication condition when compared to the on-stimulation/off-medication condition. This result shows how stimulation, even 5 years after surgery, can positively influence MPT that is significantly reduced following the device's shutdown. This finding is in line with previous studies that reported a beneficial effect of stimulation on MPT in the short-term after surgery²⁴. Even in this case, the reduction of MPT can be traced back to the underlying laryngeal dysfunction and the reduced respiratory volume mainly related to the rigidity and hypo-bradykinesia of the laryngeal and diaphragmatic muscles²³.

This study also allows for evaluation of the possible effects of dopaminergic therapy alone on speech parameters by comparing the preoperative off-medication and on-medication conditions. The results obtained did not show statistically significant differences between these two conditions, suggesting that dopaminergic therapy alone did not significantly improve or maintain speech postoperatively. These findings were consistent with previous studies that showed little or no effects of levodopa alone on acoustic speech parameters^{8,25-27}. In particular, no significant changes following levodopa intake were found in phonatory, articulatory or prosodic parameters, as previously reported²⁷ confirming the possible involvement of non-dopaminergic pathways in the pathophysiology of hypokinetic dysarthria in PD⁸.

We also found a direct correlation between the variation of speech intelligibility and tremor and PIGD subscores highlighting that the rebound of tremor and axial symptoms may worsen speech in the acute testing situation when stimulation is turned off. In addition, speech intelligibility also correlated with the UPDRS akinesia subscore in two out of the three postoperative conditions tested, highlighting a possible link between the decrease in limb movement speed and amplitude and speech. This is in line with other studies that have reported a correlation between speech variables and limb bradykinesia^{28,29}. Our study has several limitations, including a lack of definition for the position of the electrodes, the small sample size, the lack of a control group and the lack of the assessment of speech intelligibility also at the sentence level. Nevertheless, our findings highlight the possibility of positive effects of STN-DBS on speech intelligibility after surgery in the long-term. Interestingly, it also gives a better understanding of PD characteristics associated with long-term speech worsening after STN-DBS. This information may allow clinicians to improve candidates' selection for DBS and refine prognostic accuracy (e.g., GBA1 genetic status influence on speech) and that, if necessary, early speech interventions should be used after surgery in PD patients treated with STN-DBS at a higher risk of speech deterioration.

Methods

Participants. Patients treated with bilateral STN-DBS from 2012 to 2017 at the Neurological Unit of the OCB University Hospital were included. All patients fulfilled the diagnosis of PD according to the UK Brain Bank criteria³⁰ and suffered from disabling motor complications. Data from non-native Italian speakers were excluded. This study was approved by the ethics committee of the Area Vasta Emilia Nord, Italy (protocol

number: 2019/0,056,629), and written informed consent was obtained from participants. The study was performed in accordance with the Declaration of Helsinki.

Clinical assessment. The clinical evaluation was performed in accordance with the CAPSIT-PD protocol³¹. Levodopa responsiveness was evaluated through an acute levodopa challenge. Hoehn and Yahr scale (H&Y) and the Unified Parkinson's Disease Rating Scale $(UPDRS)^{32}$ were applied to quantify disease severity both in the "off-medication" condition (obtained after a 12-h antiparkinsonian medication withdrawal) and "on-medication" condition (obtained after 60 min and the administration of a 30% higher dose of the usual levodopa morning intake)³¹. Different subscores were extrapolated from the UPDRS including tremor, postural instability/gait disorders (PIGD), akinesia and UPDRS item 18 (speech) subscores. PD motor phenotype (tremor dominant [TD], indeterminate and PIGD)³³ was also extrapolated and patients were screened for the presence of mutations in the glucocerebrosidase-1 (GBA-1), leucine-rich repeat kinase-2, α -synuclein and parkin genes^{34,35}. The total amount of dopaminergic medications was calculated as levodopa equivalent daily dose (LEDD) milligrams³⁶. All patients underwent 3-Tesla brain-MRI to evaluate the presence/absence of white matter hyperintensities of vascular origin. All subjects were re-evaluated with a median five-years follow-up (range 3-7 years) after surgery. Neurological evaluation (superimposable with the preoperative one) and the speech assessment were carried out on the same day and in the following conditions: on-stimulation/off-medication (washout of at least 12-h of dopaminergic medications); off-stimulation/off-medication (stimulation was temporarily turned off for at least 1-h); on-stimulation/on-medication (stimulation was turned on and dopaminergic therapy was administered [early morning LEDD plus 30%]). Each patient underwent a complete neuropsychological assessment before surgery and at long-term evaluation, including phonemic fluency, spatial perception (localization of numbers), Raven's progressive matrices, Stroop test and Trail making test part B.

Speech evaluation. Speech evaluation was performed both preoperatively during the acute levodopa challenge and at postoperative assessment. Each evaluation was carried out in a silent environment with conversation voice intensity and was recorded with a digital voice recorder (model SONY ICDPX240) kept 20 cm from the patient's lips²⁵. The perceptual-acoustic analysis was performed using Praat software³⁷ and blinded to the patient's condition. The following tasks were included: word intelligibility (calculated as the percentage of words correctly transcribed by the examiner among a set of 25 recorded words)²⁵; oral diadochokinesis task in which participants produced the syllables /pa/, /ta/, /ka/ and the pseudoword /pataka/, as fast as they could with habitual pitch and loudness (irregular rhythm [presence of absence], uncontrolled acceleration [presence of absence]); sustained production of the phoneme /a/ for as long as possible, performed three times (duration [sec], intensity [dB]); counting from 1 to 20 (speech rate [syllables/second]). Single words intelligibility was selected due to its advantage of eliminating a number of other variables that can affect intelligibility, such as sentence level syntactic and prosodic variables. Furthermore, the use of single words to assess intelligibility is a much less difficult task for dysarthric participants than sentence level productions. As such, if an intelligibility impairment is noted at the single word level, intelligibility deficits are more than likely at higher/more complicated levels of speech productions, such as the sentence level³⁸. A calibration tone (80 SPL dB, 1 kHz) was included at the beginning of each recording to serve as a reference in the determination of speaking amplitude. According to recent guidelines³⁹, these parameters have been selected because they represent acoustic characteristics previously reported as altered in hypokinetic dysarthria^{23,27}. The presence and severity of hypokinetic dysarthria were perceptually determined by two speech language pathologists, both Italian native speakers. Speakers' severity of dysarthria was categorized on a coarse scale ranging from none, mild, moderate to severe (1: severe, 2: moderate; 3: mild: 4: none)^{40,41}.

Statistical analysis. Descriptive statistics were used for describing demographic and clinical data. The primary objective of the study was to evaluate the long-term effects of bilateral STN-DBS on speech intelligibility in advanced PD patients. As primary outcomes, we selected the change of speech intelligibility between postoperative on-stimulation/off-medication condition and preoperative off-medication condition; postoperative on-stimulation/off-medication and off-stimulation/off-medication condition. Positive changes represented improvement of speech intelligibility while negative changes represented speech worsening. The presence of significant differences in speech intelligibility in the different conditions tested was calculated using the Friedman test with subsequent post-hoc Wilcoxon signed rank test with Bonferroni correction for multiple comparisons because of the use of multiple tests (statistical adjusted significance was set at p-value < 0.005). Based on the presence/absence of long-term postoperative worsening of speech intelligibility, patients were divided into two groups ("stable/imp" [absent or positive variation] and "worsened" [negative variation]) that were compared to find significant differences in demographic, clinical and speech variables. With regards to continuous and ordinal variables, the Mann-Whitney test was used, while for categorical variables the chi-square independence test was applied (statistical significance was set at p-value < 0.05). Secondary outcomes included: the changes of the other speech variables in the different conditions tested; the correlation between the variation of speech intelligibility and the variation in the different motor scores and subscores in the on-stimulation/off-medication condition compared with the off-stimulation/off-medication condition and in the on-stimulation/off-medication compared with preoperative off-medication condition; the correlation between the different motor scores and subscores and speech intelligibility in the postoperative conditions tested. Correlation analyses were performed by using the Spearman Correlation analysis. Statistical analysis was performed using the IBM SPSS Statistics for Windows version 20.0 (IBM, Armonk, NY, USA).

Data availability

Anonymized data of this study may be available from the corresponding author upon request from any qualified researcher, following the EU General Data Protection Regulation.

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Author contributions

(1) Design of the study; (2) data collection and analysis; (3) Manuscript preparation: A. Writing of the first draft, B. Review and critique. A.G.: 1, 2, 3A; F.C.: 1, 2, 3A; I.C.: 1, 3, 3A; A.M.: 1, 3, 3A; V.Fi.: 1, 2, 3A; G.D.R.: 1, 2, 3A; B.D.: 1, 2, 3A; S.C.: 1, 2, 3A; E.B.: 1, 2, 3A; M.G.C.: 1, 2, 3A; F.A.: 1, 2, 3A; F.Ca.: 1, 2, 3A; M.A.M.: 1, 2, 3A; S.C.: 1, 2, 3A; E.M.: 1, 2, 3A; A.F.: 1, 2, 3A; A.V.: 1, 2, 3A; G.B.: 1, 2, 3B; V.Fr.: 2, 3B; S.P.: 3B; E.M.: 2, 3B; C.B.: 1, 2, 3A, 3B; F.V.: 1, 2, 3A, 3B. All authors. All authors approve the final version for publication.

Competing interests

The authors declare no competing interests.

Additional information

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