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Short communication

Effects of deep brain stimulation on spontaneous language production in people with Parkinson's disease: a preliminary study

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A R T I C L E I N F O

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A B S T R A C T

The effects of bilateral subthalamic nucleus (STN) stimulation on spontaneous language production are poorly understood. Using a pre-post surgery design, semantic and morphosyntactic parameters were evaluated according to the "Analysis of Spontaneous Speech in Aphasia" in seven people with Parkinson's disease (PD). Relative to normative data, the number of nouns and percentage of correct sentences produced were most subjective to changes over time and effects of stimulation. Twelve months after surgery, three patients with predominant left hemispheric dopamine depletion showed a normalization of the number of nouns during STN stimulation, compared to results below the norm in the bilateral OFF condition. Moreover, the effect on the percentage of correct sentences was variable, but the results remained below the norm when pre-operative deficits were present. These outcomes suggest that motor symptom laterality and pre-operative language functioning are among the variables that mediate STN stimulation effects on spontaneous language production, and emphasize the relevance to include the number of nouns and percentage of correct sentences produced as parameters in future larger-scale research.

1. Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the loss of dopaminergic nigrostriatal neurons and an α-synuclein pathology (Henderson et al., 2019). Disturbances in cortico-basal ganglia-thalamo-cortical networks lead to motor symptoms (i.e. resting tremor, muscle rigidity, bradykinesia and gait disorders; Jankovic, 2008) and to a wide range of non-motor symptoms, such as language disorders (Schapira et al., 2017). Among the latter, lexico-semantic and morphosyntactic difficulties accrue in language comprehension and production (Camerino et al., 2022; Colman & Bastiaanse, 2011; Holtgraves & Cadle, 2016). Within the available literature, the methodology is mostly restricted to investigations on word or sentence level, such that the

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obtained findings might not be transferable to daily life communication settings.

Previous studies targeting lexico-semantic and syntactic measures obtained during spontaneous language tasks (i.e. storytelling, picture description or interviews) have led to heterogeneous results. Multiple authors did not find a significant difference between people with PD (on dopaminergic medication) and healthy controls regarding the mean length of utterances (MLU), percentage of grammatically correct sentences and the proportion of complex sentences (e.g. subordination and noncanonical word order) (Dick et al., 2018; Illes, 1989; Murray, 2000; Murray & Lenz, 2001). However, Murray (2000) still reported that people with PD (on dopaminergic medication) produced more syntactically incomplete sentences (e.g. abortion of sentences) than healthy subjects. Importantly, several non-linguistic cognitive variables, such as working memory and executive (dys)functions, have been linked with and seem to influence spontaneous language production (Altmann & Troche, 2011; Auclair-Ouellet et al., 2017). Moreover, Holtgraves et al. (2010) showed that the lateralization of motor symptoms, which directly results from the asymmetric depletion of dopaminergic neurons (Djaldetti et al., 2006), can impact multiple linguistic outcome measures. In their study, PD patients (on dopaminergic medication) who had left lateralized motor symptoms (i.e. because of a predominant right hemispheric dopamine depletion/PD right) produced shorter sentences as well as fewer verbs and function words compared to PD patients with right lateralized motor symptoms (PD left).

Bilateral deep brain stimulation (DBS) of the dorsolateral (motor) area of the subthalamic nucleus (STN) is a long-term effective treatment for medication-refractory motor fluctuations in people with PD (Limousin & Foltynie, 2019). DBS of the dorsolateral STN induces modifications in structures that are (functionally) interconnected with this nucleus, through the motor cortico-basal ganglia-thalamo-cortical loop. Although the exact working mechanism of DBS remains elusive, it appears to normalize pathological bursting of the globus pallidus (pars interna), and suppress excessive beta oscillations, which leads to a reduction of motor symptoms (Ashkan et al., 2017). On the other hand, the effect of STN DBS on cognitive functions is more variable (Bucur & Papagno, 2023; Vos et al., 2021). Specific to spontaneous language, the available insights mostly stem from within-subjects cross-sectional ON-OFF stimulation designs. Batens et al. (2014) observed no significant ON-OFF differences for multiple lexico-semantic (number and variability of nouns and lexical verbs) and morphosyntactic parameters (number of copula and modal verbs, MLU, percentage of correct sentences and finiteness index). Similarly, Ehlen et al. (2020) observed no significant ON-OFF differences for sentence complexity, the use of open class words and the type token ratio (distinct lexemes/all lexemes), but fewer language errors (at various levels, e.g. lexical, grammatical, pragmatic, etc.) were detected in the ON compared to the OFF stimulation condition. On the contrary, Tiedt et al. (2021) observed no significant difference in the ratio of open to closed class words between the ON and OFF condition in patients, but, compared to a healthy control group, significantly fewer open class words were present in the OFF condition. Hence, Tiedt et al. (2021) concluded that active STN DBS led to an increase of open class words. Finally, in a group of patients with combined DBS of the STN and pedunculopontine nucleus (PPN), a trend towards a reduction of morphological and syntactic errors was present in both the STN ON – PPN OFF and STN ON – PPN ON condition compared to the STN OFF – PPN OFF condition during a template-based story generation task (Zanini et al., 2009).

The effects of STN DBS on spontaneous language of people with PD can also be assessed with longitudinal pre-post DBS surgery designs. To our knowledge, only Zanini et al. (2003) have used this design, reporting a significant reduction in morphosyntactic errors 2-3 weeks after surgery (vs. before), which persisted until 12 months after surgery. Effects on lexical-semantic parameters (e.g. the total number of words) were variable among the 4 included patients.

Given the very limited evidence on the longitudinal effects of STN stimulation on spontaneous language production, we performed a pre- and 12 months postoperative evaluation in seven patients with PD. During the post-operative evaluation, patients were tested in a bilateral ON and OFF stimulation condition. We extended the method of Zanini et al. (2003) by incorporating comparisons with normative data, enabling a novel assessment of longitudinal and stimulation-related changes in spontaneous language production relative to healthy individuals. Due to our small sample size and the paucity of prior longitudinal research on spontaneous language in this population, the current study is exploratory in nature. Based on previous (non-longitudinal) research, we hypothesized that most patients would have intact spontaneous language production before surgery (Dick et al., 2018; Murray & Lenz, 2001), although some patients could show syntactic deficits (Murray, 2000). Post-operatively, we expected bilateral STN DBS to increase the percentage of correct sentences produced (Ehlen et al., 2020; Zanini et al., 2003, 2009) compared to the condition without stimulation, but no difference between stimulation conditions for lexico-semantic parameters (i.e. the use of nouns and lexical verbs) (Batens et al., 2014; Ehlen et al., 2020; Tiedt et al., 2021).

2. Methods

2.1. Patients

Seven individuals with advanced-stage PD (two women, five men; mean age: 60.3 years, SD: 7.73 years) were included. Co-morbidity of PD and other neurological diseases was ruled out by clinical assessments and magnetic resonance imaging (MRI). All patients were native speakers of Dutch; reported no premorbid language, vision or hearing disorders; and had no history of psychiatric disorders or substance abuse. The patient sample included six right-handed individuals and one ambidexter, as determined by the Dutch Handedness Inventory (Van Strien, 1992). All patients had a left hemispheric language dominance based on the results from a dichotic listening task (Kimura, 1961). Five patients had primarily right-sided motor symptoms (i.e. predominant left hemispheric dopamine depletion/PD left), and two patients had primarily left-sided motor symptoms (i.e. predominant right hemispheric dopamine depletion/PD right), which was clear from the scores on part 3 (motor examination) of the Unified Parkinson's disease Rating Scale (UPDRS-III, Goetz et al., 2008), clinical assessments by a neurologist and the patients' subjective feeling. All patients were suitable candidates for bilateral STN DBS after extensive neurological and neuropsychological evaluations (no signs of dementia or major depression). DBS surgery took place after an average disease duration of 11 (± 2) years from the diagnosis. An overview of demographic and medical information can be found in Table 1.

2.2. Neurosurgical electrode implantation

The neurosurgical implantation of bilateral electrodes in the STN was performed using a conventional stereotactic technique, i.e. the combination of neuroimaging guided anatomical targeting, micro-electrode recordings and the clinical evaluation of macro-stimulation effects. Quadripolar electrodes (DBS lead model 3389: diameter 1.27 mm, 4 channels of 1.5 mm each and 0.5 mm interspacing between the contacts; Medtronic, Minneapolis) were used, and external stimulation was applied for at least one week before the internal pulse generator was implanted in the abdominal wall. The position of electrodes in the dorsolateral STN was verified by post-operative MRI.

2.3. Experimental procedure

All patients underwent pre- and post-operative evaluations of spontaneous language and speech intelligibility (NSVO-Z, Martens et al., 2010) in an optimal medication condition (i.e. after intake of their regular dopaminergic medication, with the dosage individually optimized by the treating neurologist as part of routine clinical care). The current manuscript is part of a more extensive study and, here, we focus on the pre-operative results (obtained approximately six months before DBS surgery) and the results collected during the bilateral ON and OFF stimulation conditions (in a randomized order) at 12 months after DBS surgery. There were at least 15 min to let patients adjust to a new stimulation condition and motor effects became clearly visible. For an overview of the medication doses, DBS settings and speech intelligibility results, see Table 2. The study was approved by the Ethics Committee of Ghent University and all patients signed an informed consent.

Spontaneous language was elicited during semi-standardized interviews without time constraints. All assessments were performed in a quiet room without distractions. The language samples were audio recorded on a Dell laptop using a condenser stereo microphone (Sony ECM-MS907) and the acoustic software PRAAT (Boersma, 2002). The questions referred to topics such as profession, family, travelling, leisure activities, general interests and their disease. A standardized approach was used to analyze lexico-semantic and morphosyntactic parameters of spontaneous language (300 words), namely the Dutch version of The Analysis of Spontaneous Speech in Aphasia (ASTA, Boxum et al., 2010). Speech intelligibility did not interfere with the transcriptions (see Table 2). At the lexico-semantic level, the number of nouns and verbs, as well as their variety (type-token ratio = number of different nouns/verbs divided by the total number of nouns/verbs) were determined. At the morphosyntactic level, the number of copula and modal verbs, MLU, percentage of correct sentences and finiteness index (i.e. the proportion of correctly inflected finite verbs) were calculated.

2.4. Statistical analysis

Results were converted to standardized z-scores to enable a comparison with the normative data of the ASTA (van der Scheer et al., 2011). The normative sample contains data of 41 healthy Dutch-speaking individuals between 18 and 78 years, and no effects of age, sex and education level were found. Z-scores larger than (minus) two were considered significantly deviating from the norm (Boxum et al., 2010). Descriptive analyses were used to characterize within-subject changes.

3. Results

Among the evaluated parameters, the number of nouns and percentage of correct sentences produced were most subjective to changes over time and effects of stimulation. For readability, we only report the results for these parameters in the following paragraphs. An overview of the z-scores for all lexico-semantic and morphosyntactic parameters obtained before and 12 months after surgery can be found in Table 3.

Number of nouns – Pre-operatively, the number of nouns produced was within the normal range ($-1.90 < z < 1.90$) in all patients

Table 1
Demographic and medical information of the seven patients.

PD	Age (years)	Sex	Disease duration (years)	Predominance motor symptoms
1	65	Male	12	Right
2	62	Male	16	Right
3	45	Female	12	Right
4	61	Male	11	Right
5	68	Female	9	Right
6	56	Male	13	Left
7	65	Male	7	Left
GA	60.3		11.4	
SD	7.73		2.88	

Note: PD = patient with Parkinson's disease, GA = group average, SD = standard deviation.

Table 2
Overview of the dopaminergic medication doses, DBS settings and speech intelligibility scores.

	PD1	PD2	PD3	PD4	PD5	PD6	PD7
LEDD (mg/day)							
Before surgery	1420	842	817	780	810	1024	1311
12 months after surgery	740	390	0	610	305	240	0
TEED (Joule)							
12 months after surgery	L: 150.43 R: 204.75	L: 53.93 R: 36.10	L: 73.71 R: 241.35	L: 104.46 R: 60.34	L: 37.61 R: 13.54	L: 187.31 R: 187.31	L: 152.55 R: 104.46
NSVO-Z (%)							
Before surgery	97	91	100	98	97	99	100
12 months after surgery (bilateral ON)	91	93	100	96	97	99	98
12 months after surgery (bilateral OFF)	96	94	97	97	98	98	99

Note: PD = patient with Parkinson's disease, LEDD = levodopa equivalent daily dose (milligrams/day), TEED = total electrical energy delivered, L = left electrode, R = right electrode, NSVO-Z = Dutch Intelligibility Assessment at sentence level (Martens et al., 2010).

(7/7, 100%). This result remained for 42.9% of the sample (3/7: PD 1, 6 and 7) 12 months after surgery. In another 42.9% of the sample (3/7: PD 3, 4 and 5), a deviation from the norm (a lower number of produced nouns) was observed during the bilateral OFF condition, whereas the bilateral ON condition led to a higher number of produced nouns, resulting in values within the normative range. Finally, in PD 2 (1/7, 14.3%), both post-operative results were below the normative range (bilateral ON: $z = -2.41$, bilateral OFF: $z = -2.03$).

Percentage of correct sentences – In 42.9% of the sample (3/7: PD 2, 5 and 7), the percentage of correct sentences produced was below the normative range before surgery. Remarkably, each of these patients remained to have results that deviated from the norm in both stimulation conditions 12 months after surgery. In PD 2, STN stimulation (ON versus OFF) was associated with a decrease in the number of correctly produced sentences (bilateral ON: $z = -3.38$, bilateral OFF: $z = -2.26$), whereas increases were observed in PD5 (bilateral ON: $z = -2.34$, bilateral OFF: -3.46) and PD 7 (bilateral ON: $z = -2.48$, bilateral OFF: $z = -5.08$).

In the remaining 57.1% of the sample (4/7, PD 1, 3, 4 and 6), no pre-operative deficits were present. In half of them (PD 1 and 4), this result remained post-operatively. Conversely, in PD 6, the percentage of correct sentences was below the norm during the bilateral OFF condition ($z = -2.34$), but normalized during the bilateral ON condition ($z = -1.61$). Finally, both post-operative findings were below the norm in PD 3, with the highest percentage of incorrectly produced sentences during the bilateral ON stimulation condition (bilateral ON: $z = -4.56$, bilateral OFF: $z = -3.96$).

4. Discussion

We set out to investigate the longitudinal effects of bilateral STN stimulation on lexico-semantic and morphosyntactic aspects of spontaneous language by using a pre-post surgery design. Given the rarity of the studied population, the sample size was small ($n = 7$), which limits statistical power and warrants cautious interpretation of the results. We acknowledge that our results should be considered exploratory rather than definitive, providing a basis for future larger-scale studies. Interpretation of the longitudinal findings should also consider the clinical context. This study was conducted within a setting of best possible clinical care, in which treatment decisions necessarily took precedence over experimental standardization. Consequently, observed changes may reflect not only the effects of DBS, but also the potential influence of other factors such as natural disease progression or adjustments in dopaminergic medication. Interactions between these factors are likely, and disentangling their individual contributions will require larger studies with sufficient power. However, the effects of DBS were assessed within each individual by comparing outcomes under DBS ON versus OFF conditions, allowing for within-subject evaluation after surgery despite the broader confounding factors. Within these constraints, our results indicate that the number of nouns and the percentage of correct sentences produced were the most prone to effects of bilateral STN stimulation.

4.1. DBS effect on the number of nouns

The neurolinguistic evaluation before surgery revealed a normal number of nouns in the entire sample. The observation of fewer nouns produced at 12 months after surgery during the bilateral OFF condition in PD 2, 3, 4 and 5 could be related to the normal progression of the disease, electrode implantation and/or the reduction in dopaminergic medication intake (Sáez-Zea et al., 2012). A post-operative reduction in dopaminergic drug use is classically observed after STN DBS surgery (Volkmann, 2004), and was also clear in our sample (Table 2). The production of less nouns co-occurred with a lower percentage of correct sentences (incomplete verb argument structures, e.g. due to an early abortion of sentences) in PD 2, 3 and 5, but they also resulted from an increased use of indefinite pronouns and fluency impairments (i.e. the frequent repetition of prepositions, (ad)verbs and pronouns). In 75% of these patients (3/4, PD 3, 4 and 5), bilateral STN stimulation led to a higher number of produced nouns, i.e.a normal result. The exact processes that were impaired in the bilateral OFF condition and recovered during bilateral STN stimulation could be linguistic (e.g. lexical retrieval, conceptualization, Silveri et al., 2012) or non-linguistic (e.g. speech, cognition) in nature (Altmann & Troche, 2011). Regarding the latter, the pre- and post-operative (ON vs. OFF) speech intelligibility scores (cf. Table 2) were similar, which at least suggests that (adaptations to) motor speech difficulties cannot (fully) explain our results. This aligns with the earlier observation of

Table 3
Raw scores and the corresponding z-scores for spontaneous language parameters of the ASTA before and 12 months after STN DBS surgery.

PD	ASTA parameter	Pre-operative	12 months post-operative	
			Bilateral on	Bilateral off
1	Number of nouns	48 (0.00)	42 (−0.76)	46 (−0.25)
	TRR nouns	0.69 (−0.91)	0.88 (1.51)	0.78 (0.28)
	Number of lexical verbs	26 (−0.72)	30 (0.24)	23 (−1.45)
	TTR lexical verbs	0.73 (0.92)	0.63 (0.03)	0.83 (1.78)
	Number of copula and modal verbs	**23 (2.65)**	20 (1.93)	16 (0.96)
	MLU	7.27 (−0.78)	5.17 (−1.99)	5.62 (−1.73)
	% correct sentences	0.84 (−1.54)	0.83 (−1.61)	0.86 (−1.21)
	Finiteness index	1.00 (0.33)	1.00 (0.33)	1.00 (0.33)
2	Number of nouns	51 (0.38)	**29 (-2.41)**	**32 (-2.03)**
	TRR nouns	0.75 (−0.19)	0.66 (−1.31)	0.69 (−0.91)
	Number of lexical verbs	26 (−0.72)	**39 (2.42)**	36 (1.69)
	TTR lexical verbs	0.62 (−0.13)	0.51 (−1.07)	0.47 (−1.43)
	Number of copula and modal verbs	12 (0.00)	17 (1.20)	8 (−0.96)
	MLU	8.15 (−0.28)	7.48 (−0.66)	7.53 (−0.63)
	% correct sentences	**0.65 (-4.72)**	**0.73 (-3.38)**	**0.79 (-2.26)**
	Finiteness index	**0.92 (-2.30)**	1.00 (0.33)	0.97 (−0.52)
3	Number of nouns	51 (0.38)	34 (−1.78)	**26 (-2.79)**
	TRR nouns	0.82 (0.79)	0.79 (0.43)	0.69 (−0.85)
	Number of lexical verbs	28 (−0.24)	22 (−1.69)	34 (1.21)
	TTR lexical verbs	0.71 (0.77)	0.59 (−0.36)	0.50 (−1.18)
	Number of copula and modal verbs	15 (0.72)	18 (1.45)	13 (0.24)
	MLU	7.47 (−0.67)	8.19 (−0.25)	6.74 (−1.08)
	% correct sentences	0.89 (−0.69)	**0.66 (-4.56)**	**0.69 (-3.96)**
	Finiteness index	1.00 (0.33)	**0.89 (-3.27)**	1.00 (0.33)
4	Number of nouns	52 (0.51)	56 (1.02)	**29 (-2.41)**
	TRR nouns	0.83 (0.84)	0.91 (1.88)	0.86 (1.28)
	Number of lexical verbs	34 (1.21)	27 (−0.48)	37 (1.93)
	TTR lexical verbs	0.74 (0.96)	0.59 (−0.34)	0.73 (0.91)
	Number of copula and modal verbs	11 (−0.24)	12 (0.00)	9 (−0.72)
	MLU	7.25 (−0.79)	7.24 (−0.80)	10.67 (1.17)
	% correct sentences	0.93 (−0.08)	0.89 (−0.59)	0.88 (−0.92)
	Finiteness index	1.00 (0.33)	1.00 (0.33)	1.00 (0.33)
5	Number of nouns	63 (1.90)	40 (−1.02)	**14 (-4.31)**
	TRR nouns	0.76 (0.02)	0.78 (0.19)	0.71 (−0.57)
	Number of lexical verbs	33 (0.97)	35 (1.45)	**50 (5.07)**
	TTR lexical verbs	0.58 (−0.49)	0.63 (−0.01)	0.54 (−0.82)
	Number of copula and modal verbs	11 (−0.24)	20 (1.93)	**28 (3.86)**
	MLU	7.50 (−0.65)	7.61 (−0.59)	6.81 (−1.05)
	% correct sentences	**0.78 (-2.54)**	**0.79 (-2.34)**	**0.72 (-3.46)**
	Finiteness index	1.00 (0.33)	1.00 (0.33)	0.93 (−1.89)
6	Number of nouns	43 (−0.65)*	37 (−1.40)	38 (−1.31)*
	TRR nouns	0.88 (1.44)*	0.89 (1.65)	0.71 (−0.68)*
	Number of lexical verbs	24 (−1.18)*	31 (0.48)	33 (1.02)*
	TTR lexical verbs	**1.00 (3.36)***	0.81 (1.60)	0.83 (1.85)*
	Number of copula and modal verbs	13 (0.34)	**21 (2.17)**	12 (0.00)
	MLU	10.09 (0.84)*	7.58 (−0.60)	**13.05 (2.54)***
	% correct sentences	1.00 (1.17)*	0.83 (−1.61)	**0.79 (-2.34)***
	Finiteness index	1.00 (0.33)*	0.97 (−0.52)	1.00 (0.33)*
7	Number of nouns	33 (−1.90)	39 (−1.14)	36 (−1.52)
	TRR nouns	0.82 (0.73)	0.82 (0.76)	0.75 (−0.13)
	Number of lexical verbs	**38 (2.17)**	28 (−0.24)	25 (−0.97)
	TTR lexical verbs	0.58 (−0.46)	0.54 (−0.86)	0.68 (0.45)
	Number of copula and modal verbs	11 (−0.24)	12 (0.00)	14 (0.48)
	MLU	9.75 (0.64)	7.81 (−0.47)	8.44 (−0.11)
	% correct sentences	**0.75 (-3.00)**	**0.78 (-2.48)**	**0.63 (-5.08)**
	Finiteness index	1.00 (0.33)	0.97 (−0.52)	0.98 (−0.50)

Note: PD = patient with Parkinson's disease, ASTA = Analysis of Spontaneous Speech in Aphasia (Boxum et al., 2010).
TTR = type token ratio, MLU = mean length of utterance, * these results are based on a sample containing less than 300 words. Standardized z-scores larger than two or below minus two were considered significantly deviating from the norm, these results are highlighted in **bold**.

nonsignificant correlations between intelligibility and spontaneous language measures (Murray, 2000). It should also be noted that it remains a matter of debate whether or not changes in language production can be fully explained by changes in cognitive functions (e.g. working memory and executive functions) or go beyond them (Auclair-Ouellet et al., 2017; Troche & Altmann, 2012). To gain insights on this specific matter, our protocol could be expanded with neuropsychological evaluations.

Interestingly, our result of a higher (and normal) number of nouns produced during STN stimulation compared to a lower (and aberrant) number of nouns produced during the condition without stimulation in PD 3, 4 and 5 seems to contradict the non significant differences between stimulation conditions in previous studies on spontaneous language (Batens et al., 2014; Ehlen et al., 2020; Tiedt et al., 2021), which could be explained by multiple methodological differences. For example, nouns were not specifically targeted by Ehlen et al. (2020) and Tiedt et al. (2021) since the authors used a combination of different open class words (i.e. nouns, lexical verbs, adjectives and modal adverbs). This could have led to certain results being averaged out. In the current study, most patients did not show a significant effect of stimulation condition regarding the use of lexical verbs, which adds to the results of Ehlen, Tiedt and colleagues. Second, between study differences in interview durations (ranging from no time restriction to 60s) and the number of words used for neurolinguistic analyses (ranging from 50 to 300 words) could have had an effect as well (Ossewaarde et al., 2020). Third, the average DBS duration was longer than 12 months for the patients included in previous studies (Batens et al., 2014, p. 3.2 ± 3.1 years; Ehlen et al., 2020, p. 3.1 ± 1.95 years; Tiedt et al., 2021, p. 2.9 ± 1.8 years). In the future, our study design could be expanded with additional evaluation moments (e.g. up to 3 years, Bucur & Papagno, 2023) to determine whether (positive) effects persist beyond 12 months. It should be mentioned, however, that although the differences were not significant, the mean number of nouns (Batens et al., 2014), open class word ratio (Ehlen et al., 2020) or open to closed class words ratio (Tiedt et el., 2021) was higher in the bilateral ON versus OFF condition in each of these previous studies. Integrating this observation with our current finding indicates that differences might be clinically relevant, despite not being statistically significant. This shows the added value of comparing patients' results with the performance of healthy controls or normative data. This is confirmed by additional results from Tiedt et al. (2021): the authors did not find a significant effect of stimulation condition, but they reported significantly fewer open class words in patients compared to a control group, and this only for the bilateral OFF condition.

Finally, we would like to highlight that the combination of an aberrant number of nouns (i.e. less) produced during the bilateral OFF condition and a higher (normal) number of produced nouns during bilateral STN stimulation was observed in 3 PD left patients, but in none of the PD right patients (PD 6 and 7). This corresponds well to the follow-up work of Batens et al. (2015), who showed a significant increase in the number of produced nouns in the bilateral ON condition in PD left patients, whereas no significant difference was present in PD right patients (Batens et al., 2015). The results of Batens and colleagues and of the current study show that even in an advanced stage of the disease, asymmetry can persist and interact with the effect of DBS on the production of nouns. Due to the limited available information on the relation between motor symptom laterality and language functioning (Steinbach et al., 2023), future studies should target this topic in two groups with equal sample sizes.

4.2. DBS effect on the percentage of correct sentences

In agreement with our hypothesis, pre-operative syntactic deficits (lower percentage of correct sentences) were present in 42.9% of the sample (3/7, PD 2, 5 and 7). Incomplete verb argument structures were produced either due to the omission of a subject or verb, or due to the early abortion of sentences. The latter replicates previous findings by Murray (2000). A lower percentage of correct sentences was observed in two PD left patients (PD 2 and 5) and one PD right patient (PD 7). Hence, no clear differences were observed based on motor symptom laterality, in contrast to Holtgraves et al. (2010) who reported shorter sentences, and fewer verbs and function words in PD right compared to PD left patients (without DBS). However, these authors excluded patients in advanced stages of the disease, which complicates a comparison with our results.

We expected bilateral STN stimulation to result in a higher percentage of correct sentences produced (Ehlen et al., 2020; Zanini et al., 2003, 2009). Off all previous studies, the experimental design of Zanini et al. (2003) corresponds the most with ours as the authors also included a pre-operative evaluation. They reported fewer morphosyntactic errors 2 weeks after surgery (bilateral ON) compared to before surgery, and a positive effect of stimulation (less errors during the bilateral ON versus OFF condition) remained until 12 months after surgery in the 4 included patients. The latter result was replicated by authors who investigated (post-operative) stimulation effects in patients with a DBS duration of 6 to 12 months (Zanini et al., 2009) or multiple years (Ehlen et al., 2020). Future research could replicate the protocol of Zanini et al. (2003) and also include a bilateral OFF stimulation condition as early as possible after surgery. This could contribute to emerging insights on the effects of stimulation versus microsurgery (Le Goff et al., 2015).

In general, between stimulation conditions changes in sentence production varied across participants, showing either (minimal) increases or decreases in z-scores. Which factors contributed to this variability remains unclear. The increased percentages of correct sentences in PD 5, 6 and 7 during the bilateral ON versus OFF condition do resemble the results of Zanini et al. (2003). However, during the bilateral on condition, only patient 6 reached a result within the normative range. This again emphasizes the advantage of using a control group. In this context, we observed that patients who had pre-operative deficits (PD 2, 5 and 7) still obtained post-operative values outside the normative range for both stimulation conditions.

Finally, it should be highlighted that the 4 patients in Zanini et al. (2003) were evaluated without dopaminergic medication, whereas all of our patients, except PD 3 and 7, were tested with medication. Regarding this matter, it is remarkable that the largest increase (15%) in percentage of correct sentences (bilateral ON versus OFF) was observed in PD 7 (PD right), who showed the largest reduction in medication intake (pre-operative: 1311 mg/day, 12 months post-operative: 0 mg/day). However, a similar result was not confirmed in patient 3 (PD left). Although our sample size is too small to make firm conclusions on this matter, there is a need for more research towards the impact of dopaminergic medication intake, symptom laterality and pre-operative language functioning on the effect of STN stimulation.

5. Conclusion

This exploratory study showed that changes over time and between stimulation conditions were most consistent for the number of nouns and the percentage of correct sentences produced. Three patients with a predominant left hemispheric dopamine depletion exhibited reduced noun production 12 months after DBS-surgery in the OFF-stimulation condition, which was restored to a normal level during bilateral STN stimulation. The result of STN stimulation on the percentage of correct sentences was variable. However, post-operative outcomes in both stimulation conditions remained below the normative range when pre-operative deficits occurred. These outcomes suggest that motor symptom laterality and pre-operative language functioning are among the variables that mediate STN stimulation effects on spontaneous language production. This work provides a preliminary basis for selecting outcome measures (i.e. number of nouns and percentage of correct sentences produced) that may help disentangle the effects of STN stimulation on spontaneous language production.

CRediT authorship contribution statement

Elissa-Marie Cocquyt: Writing – review & editing, Writing – original draft, Visualization, Validation, Formal analysis, Conceptualization. **Adrià Rofes:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization, Validation. **Katja Batens:** Methodology, Investigation, Formal analysis, Data curation, Conceptualization, Writing – review & editing. **Marijke Miatton:** Writing – review & editing, Conceptualization. **Robrecht Raedt:** Writing – review & editing, Conceptualization. **Wouter Duyck:** Writing – review & editing, Conceptualization. **Miet De Letter:** Writing – review & editing, Conceptualization. **Dirk Van Roost:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization, Resources. **Patrick Santens:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization, Resources.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used ChatGPT 3.5 to improve the readability of certain sentences. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Declaration of competing interest

The authors declare that there is no conflict of interest.

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Data availability

The authors do not have permission to share data.

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