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The effects of subthalamic nucleus stimulation on semantic and syntactic performance in spontaneous language production in people with Parkinson's disease

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ABSTRACT

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) has become an established therapeutic option for advanced Parkinson's disease (PD). In this study, the effects of unilateral and bilateral STN stimulation on spontaneous language production are explored, by comparing linguistic performance in different stimulation conditions with normative data of healthy subjects.
Language samples of ten PD patients with DBS of the STN were obtained in four stimulation conditions: bilateral stimulation on, bilateral stimulation off, stimulation of the left STN only and stimulation of the right STN only. The spontaneous language production differed from the normative data in all four stimulation conditions. Especially morphosyntactic elements of spontaneous language production were altered. Despite these linguistic

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differences with normal controls no significant differences between stimulation conditions were found. These results emphasize that the effects of STN stimulation on spontaneous language production reflect a complex interplay of multiple factors.

1. Introduction

There is increasing evidence that communication disorders in Parkinson's disease (PD) exceed motor speech disturbances and include impairments of language processing (Arnott et al., 2010; Castner et al., 2008; Copland, Sefe, Ashley, Hudson, & Chenery, 2009; Hines & Volpe, 1985; Illes, Metter, Hanson, & Iritani, 1988). Language alterations in PD affect all aspects of language comprehension and production, including morphosyntactic (Colman et al., 2009; Longworth, Keenan, Barker, Marslen-Wilson, & Tyler, 2005; Ullman et al., 1997), lexical-semantic (Angwin et al., 2009; Castner et al., 2007; Crescentini, Mondolo, Biasutti, & Shallice, 2008), and high-level language abilities (Illes, 1989; Illes et al., 1988; McNamara & Durso, 2003; Murray, 2000; Pignatti, Ceriani, Bertella, Mori, & Semenza, 2006; Zanini, Tavano, & Fabbro, 2010). Language dysfunctions are attributed to a disruption of normal functioning in the striatum and the associated neural networks of the cortico-subcortico-cortical loops (DeLong & Wichmann, 2007; Middleton & Strick, 2000), as a consequence of neurodegeneration affecting mainly the dopaminergic midbrain nuclei. The majority of subcortical language models assign cognitive control functions to these cortico-striatal networks in a general way, such as the inhibition of competing alternatives and sequencing of processes (Chan, Ryan, & Bever, 2013), although there are some studies suggesting that the basal ganglia serve a language specific function (Chan et al., 2013; Robles, Gatignol, Capelle, Mitchell, & Duffau, 2005).

Deep Brain Stimulation (DBS) has become an established therapeutic option for advanced PD with motor fluctuations that are refractory to medical treatment (Kleiner-Fisman et al., 2006; Klostermann, Krugel, & Wahl, 2012). At present, in most centers performing DBS, the subthalamic nucleus (STN) is the target of choice, as high-frequency stimulation in this nucleus improves all cardinal motor symptoms of PD, allowing a reduction of dopaminergic anti-Parkinson drug treatment (Fasano, Daniele, & Albanese, 2012). Although the exact mechanisms of DBS remain to be elucidated, it is assumed that STN stimulation alters electrical network activity within the cortico-subcortico-cortical networks, leading to an improvement of motor activity. Similar to a variety of other non-motor functions, the effects of DBS on language functions are variable, with studies showing improvement while others result in worsening of language functions. Castner et al. (2008) conducted a noun/verb generation task with STN stimulation on and off, where four probe-response settings were analyzed using the procedure proposed by Peran et al. (2003). Every probe-response setting showed different results. They found an improvement of verb generation in the noun probe – verb response condition during STN stimulation, although the errors made during STN stimulation were associated with selection constraints. Because more errors were made when more competing alternative verbs were possible. This suggests that stimulation caused problems in lexical selection of competing alternatives. Noun generation was in turn negatively influenced by STN stimulation in the noun–noun condition, without being associated with selection constraints. Because PD patients performed significantly worse with stimulation than controls in both noun–noun condition and verb–verb condition, these deficits were attributed to a general word generation deficit. Phillips et al. (2012) demonstrated in their group of early-implanted PD patients that bilateral DBS stimulation improved naming of manipulated objects in reaction time, but not in accuracy. On the other hand generation of regular verbs was negatively influenced by STN stimulation. In contrast with the above mentioned studies, Silveri et al. (2012) found that STN stimulation improved overall word generation in naming, both with higher accuracy and faster reaction times. DBS of the STN had a selective positive effect on spontaneous language production. Zanini et al.

(2003) claimed that STN stimulation increased the amount of words and reduced morpho-syntactic errors. They attributed this to a recovered equilibrium of the cortico-subcortical networks. In 2009, their findings were replicated and extended to also include morphosyntactic improvements after STN stimulation (Zanini et al., 2009).

DBS offers the opportunity to assess the effects of unilateral stimulation of the basal ganglia structures (Castner et al., 2007). The evaluation of unilateral stimulation effects on language can be particularly interesting because the cortical representation of language is strongly lateralized to the left hemisphere, especially for syntax (Dominey & Inui, 2009; Lindell, 2006; Menenti, Segaert, & Hagoort, 2012). In addition, several theoretical subcortical language models emphasize the specific involvement of left cortico-subcortical networks in language processes (Dominey & Inui, 2009; Friederici, 2011; Ullman, 2004).

PD is characterized by an asymmetric degeneration of dopaminergic depletion, resulting in lateralized motor symptomatology. The effect of an asymmetric degeneration of nigrostriatal projections and language has rarely been examined independent of general studies on cognition (Verreyt, Nys, Santens, & Vingerhoets, 2011). Holtgraves, McNamara, Cappaert, and Durso (2010) assessed the linguistic complexity of spontaneous language production by measuring sentence length and the proportion of function words and verbs. Patients with predominant right hemispheric dopaminergic denervation were found to produce significantly fewer verbs and more simplified linguistic output than patients with predominant left hemispheric dopamine depletion. Because pragmatic processes are more closely related to dopaminergic networks connected to the right frontal lobe (Jung-Beeman, 2005), they concluded that decreased linguistic complexity is a reflection of a pragmatic deficit associated with right frontal lobe dysfunction (Holtgraves et al., 2010). In another study an electrophysiological investigation was conducted on semantic comprehension of action words (De Letter, Van Borsel, & Santens, 2012). The current densities in ten predefined brain areas were measured during a covert word-reading task, on and off Levodopa administration. An increase of neural activity for semantic processing was found after Levodopa intake. Normally a bilateral symmetric distribution would be expected in healthy controls, but for some subjects the cortical activity was strongly lateralized. However, none of the patients described had higher dopamine sensitivity in the most dopaminergic depleted hemisphere, suggesting a larger dopamine-related effect on cognitive networks in the less affected hemisphere. In conclusion, both studies emphasize the different involvement of both hemispheres, reflecting asymmetrical alterations in linguistic processing related to the asymmetric degeneration of dopaminergic depletion. Together the asymmetric representation of language and the asymmetric degeneration of dopamine depletion, provide sufficient arguments to evaluate the effect of unilateral STN stimulation. To our knowledge, Schulz et al. (2012) were the first to examine language outcomes after unilateral stimulation of the STN. They assessed sentence comprehension and phonologic and semantic verbal fluency in four stimulation conditions. Bilateral stimulation deteriorated all linguistic measurements, when compared to no stimulation. Left unilateral stimulation resulted in linguistic outcomes that were inferior to those obtained by right STN stimulation. These results were related to lateralization of cognitive functions (verbal memory, lexical selection, switching and serial ordering) and to the fact that stimulation parameters are generally tuned to optimal motor responses, instead of cognitive and linguistic functioning.

Up to now, no study has been reported that examined the effects of unilateral stimulation on spontaneous language production. In this report, it is our aim to assess linguistic performance in spontaneous speech after unilateral and bilateral STN stimulation in PD, offering complementary evidence to Schulz et al., 2012, who used specific structured language paradigms. We wanted to answer the following research questions.

1. Does the spontaneous language production of PD differ semantically and morphosyntactically from that of normal subjects in any of the stimulation conditions?
2. Are any linguistic (semantic or morphosyntactic) effects of STN DBS related to lateralization of stimulation?

2. Methods

2.1. Patients

Ten men (mean age 56 years, range 41–71 years) with advanced idiopathic PD as defined by Gelb, Oliver, and Gilman (1999) were included in this study. They were all considered appropriate candidates for bilateral STN stimulation because of severe and fluctuating symptomatology affecting quality of life. Before surgery, all subjects underwent intensive neurological and neuropsychological testing. Clinical assessment and magnetic resonance imaging (MRI) indicated that there were no co-morbid neurological diseases. Neuropsychological assessment revealed no signs of dementia or major depression. None of the patients had a history of psychiatric disorders or substance abuse. Asymmetric motor symptom predominance was defined as the agreement of the motor scores of the UPDRS, the clinical diagnosis of the neurologist and the patient's subjective feelings of motor asymmetry. The clinical and demographic features are further described in Table 1. To ensure that nobody had developed dementia since DBS surgery, all patients were screened using Montreal Cognitive Assessment (MOCA) (Dalrymple-Alford et al., 2010) before inclusion in this study. All patients had bilateral STN stimulation surgery at least five months prior to testing with positive motor responses. The stimulation parameters were stable according to the neurologist and are summarized for each subject in Table 2.

Table 1
Medical and demographic features of PD patients.

Patient	Age (years)	PD duration (years)	DBS duration (months)	Motor symptoms predominance	Hand preference [a]	Language predominance[b]	NSVO-Z[c]	MOCA[d]
1	66	13	5	Right	10	Left	95%	23
2	58	10	37	Right	10	Left	99%	21
3	71	19	35	Right	10	Left	100%	27
4	56	16	12	Right	10	Left	98%	25
5	57	16	93	Right	10	Left	83%	27
6	54	10	20	Right	10	Left	98%	21
7	47	12	5	Left	10	Left	96%	25
8	57	14	7	Left	−1	Left	98%	25
9	41	13	106	Left	−6	Left	86%	23
10	57	14	65	Left	10	Left	83%	22

[a] Hand preference is measured with the Dutch Handedness inventory (Van Strien, 1992).
[b] Hemispheric language dominance is defined with the dichotic listening task.
[c] NSVO-Z = the Dutch Intelligibility Assessment at sentence level (Martens, Van Nuffelen, & De Bodt, 2010).
[d] MOCA = Montreal Cognitive Assessment (Dalrymple-Alford et al., 2010).

Table 2
Summary of the individual stimulation parameters.

Patient	Left stimulator				Right stimulator			
	Pole	Ampl (V)	Pulse width (μs)	Freq (Hz)	Pole	Ampl (V)	Pulse width (μs)	Freq (Hz)
1	1−case+	1.8	90	130	9−case+	2.2	90	130
2	1−2+	4.5	90	130	5−case+	4	90	130
3	3−case+	3.7	90	130	6+7−	2.5	60	130
4	2−3−	2.5	90	130	9−10−11+	2.7	90	130
5	1−2+	5.3	90	130	7+6−5−	5	90	130
6	2−3−case+	1.8	90	130	8+9−10−11+	3	90	130
7	0−1−	2.2	90	130	10−11−	2.6	90	130
8	1−case+	3	60	130	9−case+	3	60	130
9	1−2−	2	90	130	2−case+	1.1	60	130
10	3+2−	4	90	130	7+6−	4.3	90	130

Ampl = amplitude; Freq = frequency.

2.2. Neurosurgery

The neurosurgical placement of electrodes in the STN was done using a conventional stereotactic technique, with indirect targeting combining atlas coordinates, micro-electrode recording and intra-operative macro-electrode stimulation to determine optimal location of stimulation contacts.

Tetrapolar electrodes (Medtronic 3389, Medtronic, Minneapolis) were implanted and external stimulation was done for at least one week before implantation and connection to the pulse generator in the abdominal wall.

2.3. Neurolinguistic analysis

Patients were all native Dutch speakers, who reported no premorbid language disorders, vision or hearing problems. Handedness was determined by the Dutch Handedness inventory (Van Strien, 1992) for which scores may range from −10 for extreme left-handedness until +10 for extreme right handedness: eight patients were completely right handed (+10), one moderately left handed (−6) and one ambidextrous (−1). The hemispheric language predominance was defined by means of a dichotic listening task (Kimura, 1961).

The speech intelligibility of all subjects was judged using the “Nederlandstalig spraakverstaanbaarheidsonderzoek zinsniveau” (NSVO-Z), the Dutch version of “Dutch Intelligibility Assessment at sentence level” (DIA-S) (Martens, Van Nuffelen, Van den Putte, Wuyts, & De Bodt, 2010), in order to verify that speech intelligibility was not an interfering factor for reliable transcriptions of the language samples. NSVO-Z is a computer program that randomly selects 18 nonsense sentences from a database containing 1200 sentences, blinded from the test evaluator. The subject was asked to read the sentences aloud while being recorded. Next, all sentences were transcribed and compared to the target sentences. The intelligibility score was calculated as the percentage of correctly identified words. For people under the age of 70, a score lower than 96% is considered to be dysarthric. Above the age of 70, a score below 93.1% is labeled dysarthric. Subjects with a NSVO-Z score lower than 80% were excluded from this study.

The language analysis was conducted using the standardized method for quantitative analysis of spontaneous language production from the ‘Analysis of Spontaneous Speech in Aphasia (ASTA)’ (Boxum, van der Scheer, & Zwaga, 2010) in order to be able to refer to the normative data of the ASTA (van der Scheer, Zwaga, & Jonkers, 2011). The ASTA describes how to collect, transcribe and analyze spontaneous language samples. The language samples are obtained by means of a semi-standardized interview without time constraints. The subjects are asked to answer open-ended autobiographical questions. The questions were referring to topics such as work, family and housing, traveling, leisure and general interests. At least three different topics were addressed during a single interview. The first 300 words of each interview were orthographically transcribed for analysis.

Semantic analyses were conducted by counting the amount of nouns, the amount of lexical verbs, the variety of nouns and the variety of lexical verbs (type-token ratio). Morphosyntactic evaluation was conducted by counting the amount of copula and modal verbs, mean length of utterance (MLU), percentage of correct sentences and finiteness index (proportion of correctly inflected verbs on the total number of clauses containing a verb).

In order to be able to interpret the results of the present study, some knowledge about syntactic construction of the Dutch language is required. In Dutch, copula and modal verbs are highly frequent and irregular verbs. They are accounted as closed-class words that contain hardly any lexical information (Bastiaanse, 2011). Lexical verbs are open-class words that have a lexical and a grammatical function in a sentence, determining the sentence structure and relationships with time and agreement (Altmann & Troche, 2011).

All transcriptions and analyses were independently done by two experienced speech pathologists (KB and SV). Subsequently, the results were compared and mutual consensus was reached in case of a discrepant judgment.

The patients were assessed in four STN stimulation conditions: bilateral stimulation on, bilateral stimulation off, only stimulation of the left STN, only stimulation of the right STN. To avoid order or sequence effects within subjects, conditions were randomized. The patients maintained their optimal doses of medication during testing. After switching to a new stimulation condition, there was at least a fifteen-minute break to ensure the patient was adapted to the new condition and motor effects of stimulation changes were visible. Stimulation parameters were those for which the subjects experienced optimal clinical benefits.

All audio samples were recorded digitally on a notebook (Dell laltitude e6500) using a condenser stereo microphone (Sony ECM-MS907) and the acoustic software Praat (Boersma, 2002). Recording took place in a quiet room without distractions.

Patients were aware of the study aims and agreed by signing an informed consent. This study was approved by the Ethical Committee of Ghent University.

2.4. Statistical analysis

All statistical analyses were performed in SPSS 21 for Windows. Normal distribution of the dataset was visually explored with Q–Q plots and confirmed by a Kolmogorov–Smirnov test. The linguistic measures of our PD group in the four stimulation conditions were compared with the normative data of the ASTA via a one-sample *T* test. *P*-values less than 0.05 were considered to be significant. The eight linguistic variables in the four stimulation conditions were compared with each other using a linear mixed model. Due to multiple comparisons, a Bonferroni correction was applied in the linear mixed model whereby *P*-values less than .006 (0.05/8) were considered significant.

3. Results

There was one ambidextrous person and one left handed person. The dichotic listening test indicated that the left hemisphere was the language dominant hemisphere for all PD patients. Four out of ten patients were labeled dysarthric based on the NSVO-Z results. A summary of the results of the Dutch Handedness inventory, the NSVO-Z and the dichotic listening task can be found in Table 2.

3.1. Linguistic characteristics of spontaneous language production in PD in the four stimulation conditions

To obtain an overall impression of the linguistic characteristics of spontaneous language production in PD, all linguistic variables of our PD group were compared for each stimulation condition with the normative means of the ASTA (Table 3).

Table 3
Descriptive data of the overall PD group, the mean score of the ASTA normative data and the results of the on sample *t*-test in all stimulation conditions.

	Stimulation condition	Mean ASTA	Mean PD	Stand. Dev	*t*	*p*	95% Confidence Interval of the difference	
							Lower	Upper
Amount of nouns	Bilateral off	48	40.4	9.82	−2.447	.037*	−14.6269	−.5731
	Bilateral on	48	43.2	6.55	−2.319	.046*	−9.4824	−.1176
	Only left	48	39.3	6.14	−4.475	.002*	−13.0975	−4.3025
	Only right	48	43.7	9.76	−1.393	.197	−11.2851	2.6851
TTR nouns	Bilateral off	.76	.748	.126	−.301	.770	−.1022	.0782
	Bilateral on	.76	.736	.105	−.720	.490	−.0994	.0514
	Only left	.76	.784	.074	1.032	.329	−.0286	.0766
	Only right	.76	.746	.107	−.415	.688	−.0904	.0624
Amount of lexical verbs	Bilateral off	29	28.3	4.42	−.500	.629	−3.8643	2.4643
	Bilateral on	29	29.1	5.15	.061	.952	−3.5856	3.7856
	Only left	29	29.2	4.73	.134	.897	−3.1857	3.5857
	Only right	29	30.5	5.95	.797	.446	−2.7556	5.7556
TTR lexical verbs	Bilateral off	.63	.716	.074	3.684	.005*	.0332	.1388
	Bilateral on	.63	.659	.043	2.142	.061	−.0016	.0596
	Only left	.63	.678	.124	1.226	.251	−.0406	.1366
	Only right	.63	.683	.157	1.064	.315	−.0597	.1657

Table 3 (*continued*)

	Stimulation condition	Mean ASTA	Mean PD	Stand. Dev	t	p	95% Confidence Interval of the difference	
							Lower	Upper
Amount of copula and modal verbs	Bilateral off	12	16.6	6.11	2.379	.041*	.2265	8.9735
	Bilateral on	12	15.1	5.95	1.647	.134	−1.1582	7.3582
	Only left	12	18.5	4.33	4.750	.001*	3.4047	9.5953
	Only right	12	13.6	5.04	1.004	.341	−2.0037	5.2037
MLU	Bilateral off	8.63	7.17	.924	−4.982	.001*	−2.1172	−.7948
	Bilateral on	8.63	7.94	2.11	−1.029	.330	−2.1999	.8239
	Only left	8.63	7.99	.943	−2.152	.060	−1.3170	.0330
	Only right	8.63	7.56	2.18	−1.543	.157	−2.6285	.4965
% correct sentences	Bilateral off	.93	.717	.149	−4.532	.001*	−.3193	−.1067
	Bilateral on	.93	.751	.056	−10.096	.000*	−.2191	−.1389
	Only left	.93	.689	.122	−6.234	.000*	−.3284	−.1536
	Only right	.93	.723	.128	−5.122	.001*	−.2984	−.1156
Finiteness index	Bilateral off	.99	.949	.024	−5.388	.000*	−.0590	−.0241
	Bilateral on	.99	.942	.055	−2.739	.023*	−.0875	−.0083
	Only left	.99	.953	.024	−4.795	.001*	−.0538	−.0193
	Only right	.99	.961	.057	−1.607	.142	−.0703	.0119

TTR = type token ratio; % correct sentences = percentage of correct sentences; MLU = mean length of utterance; Stand. Dev = standard deviation.* $p < 0.05$.

When comparing the mean results of the different stimulation conditions to normative means, the condition with STN stimulation off gave the largest amount of deviant linguistic parameters. PD patients produced significantly fewer nouns and there was a larger diversity of lexical verbs in the condition ‘STN stimulation off’. On top, all syntactic variables deviated from normative values of the ASTA in the condition ‘STN stimulation off’. The PD group generated, in the condition with STN stimulation off, significantly more copula and modal verbs. The MLU was smaller and the amount of correct sentences reduced. Finally, the finiteness index was lower than the normative value.

The condition ‘bilateral STN stimulation on’ resulted in a deviation from normative means in terms of a lower production of nouns, a lower percentage of correct sentences, and a lower finiteness index. In the condition with only stimulation of the left STN, a lower amount of nouns, a higher amount of copula and modal verbs, a lower percentage of correct sentences and a lower finiteness index, were registered compared to normative values. Finally, in the condition with stimulation of the right STN only a lower percentage of correct sentences in comparison to the normative data was found.

3.2. *Effects of stimulation*

In terms of stimulation effects, none of the linguistic variables varied significantly across the four stimulation conditions (Table 4).

Table 4
Comparison of linguistic variables in the different stimulation conditions (linear mixed model).

Differences in stimulation conditions	p-value
Amount of nouns	.564
Type token ratio nouns	.706
Amount of lexical verbs	.771
Type token ratio lexical verbs	.628
Amount of copula and modal verbs	.190
MLU	.537
Percentage correct sentences	.486
Finiteness index	.687

MLU, mean length of utterance.

4. Discussion

The present study aimed to provide a more detailed description of the linguistic features of spontaneous language production in PD, under different STN stimulation conditions.

4.1. Linguistic characteristics of spontaneous language production in PD (STN stimulation off)

The current study corroborates previous research findings (Illes et al., 1988; Zanini et al., 2009, 2010) indicating an overall morphosyntactic deficit. PD patients produced shorter and more incorrect sentences than healthy subjects. A smaller MLU indicates a reduction in grammatical complexity (Borovsky, Saygin, Bates, & Dronkers, 2007; Murray, 2000), supporting the suggestion that the cortico-striatal loops are involved in the processing of complex and ambiguous sentences (Dominey & Inui, 2009).

Although the amount of nouns is usually seen as a semantic parameter, the reduced amount of nouns can be explained in terms of their grammatical function (Grossman et al., 2003; Peran et al., 2003). Nouns obtain a thematic role in a grammatical structure and can be partially replaced by function words, which are close class words. This is in contrast with verbs who have a dominant role in sentence generation and function as an assigner of thematic roles (Altmann & Troche, 2011). Sentences are built around verbs. Therefore, the vast majority of sentences in spontaneous language production have to include a verb. It has been suggested that in order to be able to assign thematic roles, patterns of activity within a recurrent prefrontal network are necessary (Bates, McNew, Macwhinney, Devescovi, & Smith, 1982; Dominey & Inui, 2009). The resulting patterns need to be encoded by the striatum to map open class elements, like nouns, onto their appropriate thematic roles (Hinaut & Dominey, 2013). Reduced noun production can therefore be the result of morphosyntactic difficulties due to dysfunctional cortico-striatal networks.

The reduced amount of nouns is in contrast with a previous study on the use of nouns and verbs in spontaneous language production (Pignatti et al., 2006), where no differences between PD and healthy controls were found. The discrepancies between the outcomes of both studies are difficult to explain, as the methodologies are quite similar. The lack of more detailed information on the PD population in the Pignatti et al. (2006) study precludes a full comparison of both reports.

To our knowledge, the present study is the first study dissociating lexical verbs from copula and modal verbs in PD language analysis. Also the enlarged use of copula and modals confirms the presence of morphosyntactic difficulties. By replacing lexical verbs by high frequent, irregular, non-lexical verbs, PD patients avoid inflection of lexical verbs. Verb inflection deficits in PD have been described before and the diminished finiteness index supports the idea of verb inflection deficits (Colman et al., 2009; Longworth et al., 2005; Ullman et al., 1997). On the other hand, because copular and modal verbs are grammatical close class words, the overuse can be a compensatory mechanism to facilitate grammatical role assignment and postpone the mapping of open class words onto the grammatical structure to the rear end of that grammatical structure (Bastiaanse, 2011; Hinaut & Dominey, 2013).

Beside the morphosyntactic deficits, the spontaneous language production is probably influenced by more general cognitive dysfunctions. The increased variety of lexical verbs can be explained in that perspective. A possible underlying cause of language disturbances in PD studies is the impairment in inhibition and selection of competing alternatives. Because verbs have more lexical alternatives than nouns, they are probably more vulnerable to inhibitory disturbances (Peran et al., 2003). The suppression and selection of irrelevant and relevant alternatives demands balanced levels of dopamine, not only in the striatum but also in the prefrontal cortex. Imbalance within cortico-subcortical circuits can lead to a disturbance of competition and inhibition (Crescentini et al., 2008; Fallon, Williams-Gray, Barker, Owen, & Hampshire, 2013; Silveri et al., 2012), causing increased competition among lexical verbs in PD.

4.2. Effects of stimulation

No consistent differences were found between stimulation conditions across the different linguistic parameters. Despite the fact that no stimulation interactions were statistically detectable, the mean scores of the linguistic parameters clearly deviate from the normative values, depending on the stimulation condition. This does not rule out the possibility that spontaneous language production might be influenced by stimulation effects, but perhaps these effects are averaged out, due to additional variables (e.g. demographic and medical parameters) that might interact with the effect of STN stimulation of each PD patient and who are quite homogenous in our study group. Unfortunately, there is no data available to estimate the interaction of these variables on language production.

One of the variables that possibly interacts with the linguistic outcome is the lateralization of the nigrostriatal degeneration. In this study the asymmetric characteristic of PD is not taken into account and both PD patients with primarily left-sided and right-sided motor disturbances were included in this study. Prior studies found a correlation between the asymmetric degeneration of nigrostriatal networks and the strongly lateralised cortical representation of language (De Letter et al., 2012; Holtgraves et al., 2010).

Also stimulation parameters are known to influence the outcome of DBS. Stimulation parameters that are beneficial for motor function, which are of primary interest for the treating physicians, do not necessarily correspond to the optimal parameters for cognitive function or speech (Hershey et al., 2008; Tripoliti et al., 2008). Another consideration is that the localization of the electrode within the STN, with a resulting effect on different somatotopically arranged areas within the motor part of the STN, can influence the results (Tripoliti et al., 2008).

Although the different stimulation conditions only results in deviations compared to normative data and interpretation should be done with care, these explorative data may provide indications and suggestions for further research.

The highest number of linguistic variables outside the range of healthy control were found in the off-stimulation condition, suggesting that linguistic deficits might be inherent to PD pathology. Yet, the effect of STN stimulation varies depending on the measured linguistic parameter indicating that the linguistic deviations are caused by different underlying mechanisms. First, it confirms the idea that DBS stimulation has task-specific effects and the outflow pathways are affected differently depending on the task (Schulz et al., 2012; Thobois & Broussolle, 2012; Thobois et al., 2007). Second, it stresses the complex interplay of linguistic and non-linguistic elements in spontaneous language production.

No studies have been performed on the lateralized effect of STN stimulation on spontaneous language production. Our data indicate that there seems to be an effect on some linguistic outcomes, depending on the side of stimulation. Stimulation of the left STN results in less morphosyntactically correct sentences with more modals and copula, less nouns and more mistakes in verb inflection in comparison with the conditions “bilateral stimulation on” and “only stimulation of the right STN”. For all subjects, the left hemisphere was assigned to be the language dominant one. It has been suggested that STN stimulation has a negative effect on the hemisphere specific language functions (Holtgraves et al., 2010). The negative effect of the left STN is parallel with findings on speech disturbances (Santens, De Letter, Van Borsel, De Reuck, & Caemaert, 2003; Tripoliti et al., 2011), and previous linguistic work (Schulz et al., 2012). Stimulation of the left STN seems to interfere with left (sub)cortical networks which are largely associated with morphosyntactic functions (Friederici, Kotz, Werheid, Hein, & von Cramon, 2003; Kotz, Schwartze, & Schmidt-Kassow, 2009). Once the right STN is stimulated as well, language production seems to normalize. When the right STN is stimulated alone, all parameters normalize except the percentage of correct sentences. This is consistent with the idea that the left basal ganglia are involved in syntactic processes (Dominey & Inui, 2009).

5. Conclusion

The spontaneous language production of PD patients contains more morphosyntactic errors than healthy subjects. The effects of STN stimulation seem to be highly individual. The findings of this study are a confirmation of the complexity of language disturbances in PD. It underscores once again the multifactorial interaction of cortical and subcortical structures in semantic and syntactic aspects of production and the long road ahead to unravel these processes. Further research will need to focus on disentangling all influencing factors, with a special emphasis on laterality of cortico-subcortical effects in spontaneous language production.

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