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# Language Processing in Parkinson's Disease Patients Without Dementia

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## 1. Introduction

One of the major pathophysiological features in Parkinson's disease, from now on referred to as PD, is the loss of dopaminergic neurons in the substantia nigra, which in turn results in dysfunction of the cortico-striato-cortical circuits (Bartels & Leenders, 2009). In PD the components of the cortico-striato-cortical circuits are not in an optimal interaction, leading to insufficient engagement of for example the frontal and prefrontal lobes. Motor symptoms of tremor, bradykinesia, and rigidity are the clinical hallmark of PD (Wolters & Bosboom, 2007), however, non-motor symptoms are often present (Dubois & Pillon, 1995, 1997). In particular cognitive impairments in the domain of executive functioning have frequently been observed, both in late and also in very early stages of PD (Muslimovic et al., 2005). The term 'executive functioning' is used as a blanket term referring to a set of abilities that allow individuals to achieve goal-oriented behavior. These aspects of behavior can be regarded as top-down processes, in contrast to bottom-up processes that only represent stimulus-driven processing. Strauss et al. (2006) defined executive functioning as a collection of processes that are responsible for guiding, directing, and managing cognitive, emotional and behavioral functions, particularly during active, novel problem solving. As PD progresses, more severe cognitive impairments or dementia can occur (Aarsland et al., 2003). The dementia in PD exhibits normal or only slightly decreased performance in gnosis and praxis functions, and is typically characterized by a progressive dysexecutive syndrome with disturbed memory functions and attention (Dubois & Pillon, 1997).

In addition, it has repeatedly been shown that language functions in PD patients with dementia are affected. Demented PD patients show reduced verbal fluency, poor confrontation naming abilities, decreased word list generation, and difficulties in word-finding (Dubois & Pillon, 1997; Pahwa et al., 1998). However, prior to dementia, PD patients also evidence subtle language impairments. The question whether the language system itself is impaired, as for example in aphasia, or whether language performance is disrupted because of non-linguistic executive function disorders in PD is still unanswered. We assume that, intact executive functioning is a prerequisite for normal language functioning. Therefore, language processing deficits in PD will always be associated with executive function deficits. Under this view, the language faculty is not considered to be totally modular in nature, but thought to depend on other cognitive functions, since, for example, comprehending a sentence demands that a listener flexibly guides his/her attention to relevant linguistic information, maintains information in working memory during the

incremental development of the sentence interpretation and inhibits prepotent or incorrect parsing. This raises the question which aspect(s) of executive functioning are most important for language comprehension.

The studies described in this review reported on PD patients’ production and comprehension in several languages (English, French, German, Greek and Dutch). From the literature it is clear that PD disrupts the processes involved in both language production and language comprehension.

In the present chapter, we will use Levelt's framework for sentence processing (1983, 1989) to clarify production and comprehension of spoken language. This includes implementation of the distinction between controlled and automatic cognitive processing. Figure 1 depicts Levelt’s “Blueprint for the speaker” and shows the complex architecture of the various processes involved in speech production and comprehension.

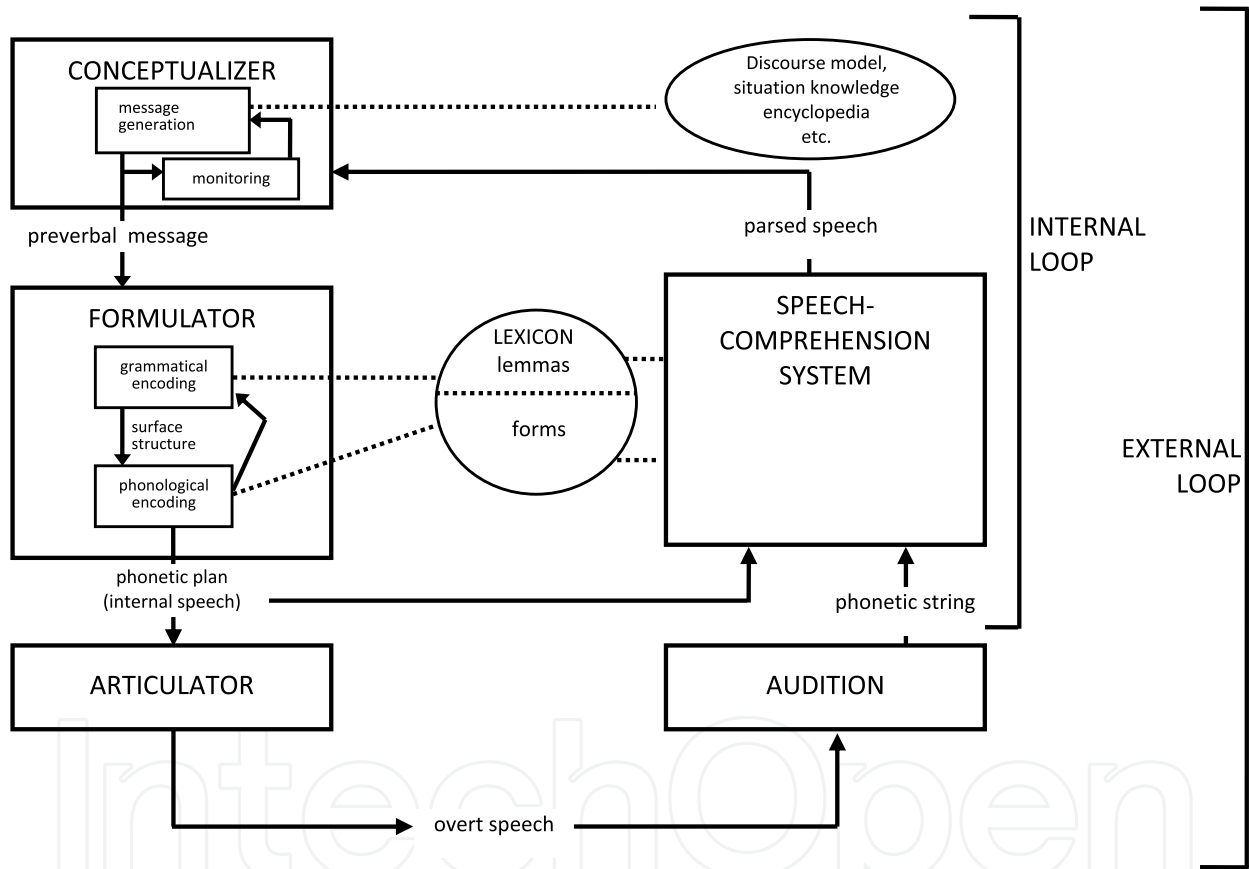


Fig. 1. Blueprint for the speaker (Adapted from Levelt, 1989)

In this figure, the boxes represent processing components and the circle as well as the ellipse represent knowledge stores. The framework consists of two subsystems, one for production and one for comprehension. The Production System is further divided into a Conceptualizer, a Formulator and an Articulator. When a speaker produces speech, he starts with an idea that he intends to communicate in the Conceptualizer. Conceptualizing demands working memory (Levelt, 1989), since during this stage an intention needs to be conceived and relevant information needs to be retrieved from long-term memory and ordered while keeping track of the discourse. In short, the Conceptualizer provides an interface between thought and language and produces a pre-verbal message. Then, using

two steps, the Formulator translates this pre-verbal message into a linguistic structure. In a first step, the Grammatical Encoder must access lemma information<sup>1</sup> from the mental lexicon (i.e., declarative knowledge) and activate syntactic building procedures stored in the Grammatical Encoder (i.e., procedural knowledge). Based on the properties of the message, the Grammatical Encoder will assign grammatical functions to the words and build a phrasal representation (e.g., verb phrases or noun phrases), specifying the hierarchical relation between syntactic constituents and their linear order. In a second step, the Phonological Encoder fills in the word forms in the structure that was generated by the Grammatical Encoder. It then constructs a phonetic plan, which is transformed into a spoken utterance by the Articulator. Formulation is “a largely automatic process” (Levelt, 1989, p. 21), implying that lexical retrieval and syntactic planning during production do not rely much on executive functions. However, declarative and procedural memory are both not disconnected from executive functions. For example, during the course of syntactic structure building the selected lemmas from declarative memory need to be maintained and updated by executive functions until the process is terminated.

On the right-hand side in Fig. 1, the Speech Comprehension System is depicted. During comprehension, a spoken utterance is mapped to a phonetic string by the Audition component, from which the Speech Comprehension System computes parsed speech, a representation of the input in terms of phonological, morphological, syntactic, and semantic composition. This representation is further processed by the Conceptualizer. Sentence parsing during comprehension is constrained by working memory capacity (Caplan & Waters, 1999; Just & Carpenter, 1992; Just et al., 1996; Waters & Caplan, 1996).

Speakers inspect their overt and covert speech for errors, thereby allowing themselves to inhibit and repair erroneous utterances. As Levelt (1989, p. 13) says, “a speaker is his own listener”. Levelt localizes the central Monitor in the Conceptualizer (see Fig. 1). Very much simplified, Levelt’s framework proposes that during language production the speaker monitors production through the Comprehension module. This proposal is known as the ‘perceptual loop theory of speech monitoring’, and claims that a speaker’s phonetic plan is processed by the Speech Comprehension System during speech production, which allows the speaker to compare the comprehension of what he is about to say (‘the internal loop’) to what he originally intended to express. Speakers are also hypothesized to listen to their own overt speech, giving them another chance to detect errors (‘the external loop’). In that case, they use the Audition component to analyze their own speech. Both feedback loops will reach the Monitor located in the Conceptualizer, which checks whether the parsed speech matches the intended speech. Upon error detection, the Monitor signals the speech production system to interrupt speech and to plan a repair process. The Monitor in Levelt’s framework has been described as being a central, conscious process that oversees end products of speech production (Postma, 2000). Analogously to the monitoring system in speech production, Van Herten (2006), Van Herten et al. (2006), Vissers (2008), and Van de Meerendonk et al. (2009) proposed a monitoring process during comprehension inspired by the conflict monitoring theory of Botvinick et al. (2001). In the same line, Kuperberg (2007) suggested a monitoring process embedded in her non-syntactocentric, dynamic model of language processing.

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<sup>1</sup> The lemma of a word contains the semantic and syntactic information, necessary for the construction of the syntactic structure of the sentence. A lemma is still very abstract and distinct from the word forms, that are stored at a different level in the Lexicon

This chapter presents an overview of the extensive and still growing literature examining the underlying mechanisms of the subtle language impairments in non-demented PD patients. The connectivity of the basal ganglia with especially the frontal cortical regions explains why language processing is a vulnerable cognitive function in the course of PD. We start with reviewing what is known about language production deficits in non-demented patients with PD, followed by a summary of the receptive language deficits in PD. This review will not be limited to deficits at the sentence level, but will also consider deficits at the word and discourse level. Over the years, a variety of methodologies have been used, and recently functional imaging in PD patients has begun to add information to the neural instantiation of the patients' language impairments. Studying language processing in PD allows researchers to analyze the effects of poorly functioning, yet still engaged cortico-striato-cortical circuitry during language performance. Some of the studies reviewed in this chapter aimed at examining language processing in PD, to ultimately define the role of the basal ganglia in language processing (e.g., Ullman et al., 1997; Friederici et al., 2003; Grossman et al., 2003; Kotz et al., 2003). In the final section of this chapter, advice for communication guidelines that would guarantee a better quality of life for patients suffering from PD is given. The chapter will be concluded with suggestions for future research on language processing in PD.

## **2. Language production in PD**

### **2.1 Spontaneous speech**

Spontaneous speech in PD patients is often characterized by hypokinetic dysarthria and hypophonia, joined in the term 'dysarthrophonia' (Ackermann & Ziegler, 1989). Some PD patients in the advanced disease stage produce repetitions of speech, which are also labeled as stuttering, speech iterations, or palilalia (Benke et al., 2000). The major complaints reported by PD patients are not as much related to the acoustic, perceptual and physiological changes to their speech, but are related to the effect of these changes on communication overall, their view of themselves and the detrimental effects of the effort required to overcome physical and mental limitations (Miller et al., 2006). Also, PD patients' prosody, facial expression and gestures are abnormal, probably because these are influenced by the cardinal motor impairment.

One of the focuses of this review on language processing is grammatical effects in the spontaneous speech of PD patients, which were first reported by Illes et al. (1988). The sentences produced by the moderately impaired PD patients were syntactically simple. The pattern may reflect an adaptive, compensatory mechanism to reduce speech-motor difficulty, or may actually be evidence of a language impairment intrinsic to the disease process. Illes and colleagues (Illes, 1989; Illes et al., 1988) favored the adaptation hypothesis, stating that as the severity of the disease and, hence, the dysarthria increases, PD patients adapt to or compensate for their motor speech difficulties. Using a verbal picture description task, Murray (2000) observed compromised grammar and informativeness of spoken language in PD patients. Furthermore, a relationship between syntactic changes in production and concomitant cognitive changes was found. While analyzing conversational speech, Murray and Lenz (2001) found that patients with greater cognitive deficits and dysarthria performed more poorly on syntactic measures than patients with either more intact cognitive abilities or more intelligible speech. They suggested that PD patients show syntax limitations in production, but only under certain task requirements or related to



other cognitive deficits. This conversational speech analysis showed that changes in language production in PD reflect concomitant cognitive and motor speech impairments, rather than being a pure language deficit. Ellis et al. (2006, see also Ellis, 2006 and Ellis & Rosenbek, 2007) analyzed narrative discourse in individuals with PD and in healthy control speakers. According to Ellis et al. (2006) the analysis of narrative discourse is as a method to differentially characterize expressive language form versus use<sup>2</sup>. They concluded that patients with mild to moderate PD demonstrate deficits in language use while maintaining spared language form.

Earlier, McNamara et al. (1992) suggested that mildly to moderately impaired PD patients have a reduced capacity to simultaneously speak and monitor one's own speech resulting in self-monitoring impairments during narrative discourse. To test overt speech monitoring in narrative discourse of patients with PD, they used the procedures of the Cookie Theft picture description task of the Boston Diagnostic Aphasia Examination (BDAE, Goodglass & Kaplan, 1972). The number and the distribution of uncorrected errors and two repair types were tallied. The results showed that PD patients made three times more errors than the age-matched control speakers and used both repair strategies, but relatively less often than the control speakers. According to the authors, this significant unawareness of speech errors is related to attentional dysfunctioning in PD. They furthermore suggested that PD patients display reduced sensitivity to context, which may complicate their language comprehension. In order to explicitly evaluate PD patients' pragmatic skills<sup>3</sup>, McNamara and Durso (2003) used a formal pragmatic communication skills protocol (Prutting & Kirchner, 1987). The pragmatic communication skills were also rated on the basis of the assessment of (self-)awareness of the problem by individual PD patients and their spouses. It was concluded that PD patients were significantly impaired on measures of pragmatic communication abilities and were less aware of their communication problems. In line with Levelt's framework (1989, see Fig. 1) it is concluded that PD patients have a problem in their monitoring system and, thus, are not aware of their errors or, in other words, do not detect the mismatch when comparing their intentions and the actual speech output.

## 2.2 Verb production in sentence context

In 1997, Ullman and colleagues obtained evidence for a role of the basal ganglia in morphosyntactic production. Ullman et al. (1997) reported the results of a sentence completion task, which required the participants to read aloud randomly ordered sentence pairs and to fill in a past tensed verb. The authors found a correlation between right-side hypokinesia and the impaired production of rule-generated (regular) past tense forms in PD. The authors concluded that PD leads to the suppression of both motor activity and grammatical rule application. In essence, Ullman et al. (1997) and Ullman (2001) proposed that the frontal basal ganglia system, which is damaged in PD, constitutes the procedural memory system that regulates grammar (Grammatical Encoder in Fig. 1) and that the

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<sup>2</sup> In defining 'what is language', Bloom and Lahey (1978) divided language into three different, but overlapping aspects: content, form and use. In brief, language content includes factors such as semantics, including word knowledge and world knowledge, and vocabulary. Language form refers to the grammar of the language, while language use is akin to the area of pragmatics.

<sup>3</sup> Pragmatic skills involve the ability to use and interpret verbal and nonverbal language appropriately within the social context in which communication occurs, requiring a degree of inference and interpretation (Perkins, 2005).

mental lexicon depends on declarative memory (see Fig. 1), embedded in the temporal lobe, which is largely intact in PD. Set in Levelt's framework (Fig. 1), it is proposed that PD patients have a deficit in grammatical encoding. As a result, PD patients are not able to produce the past tense form of regular verbs.

In the following years, the vast majority of studies on verbal morphosyntactic production in PD focused on testing the Declarative-Procedural hypothesis of Ullman et al. (1997), but the PD data of the Ullman study could not be replicated (Almor et al., 2002; Longworth et al., 2003; Longworth et al., 2005; Penke et al., 2005; Terzi et al., 2005). Longworth et al. (2005) found a tendency in English-speaking PD patients (among other patients with striatal damage) to perseverate on the cue (i.e., verb stem) rather than to produce past tense verbs as requested. Longworth et al. (2005) argued against an isolated grammatical deficit in PD and suggested that the striatum plays a general (i.e., not specific to language), inhibitory role in the later, controlled stages of language comprehension and production. The deficits in PD may reflect impairment of inhibition of competing alternatives during the later controlled processes involved in both comprehension and production (Longworth et al., 2005). Related is our evidence for executive dysfunctions being correlated to deficits in verb production in sentence context (Colman et al., 2009). Contrary to the findings of Ullman et al. (1997), but consistent with the findings of Longworth et al. (2005), no influence of regularity on verb production in sentence context was detected in the Dutch-speaking PD patients. In a study on verb production in sentence context, we showed that a deficit with regular inflection is not a characteristic for Dutch-speaking PD patients (Colman et al., 2009). We furthermore suggested that because of failing automaticity, PD patients relied more on the cortically represented executive functions. Unfortunately, due to the disturbed intimate relation between the basal ganglia and the frontal cortex, these executive functions are also dysfunctional. We manipulated the grammatical features of the test sentences, in order to simultaneously test verb retrieval and sentence integration processes in a group of PD patients compared to a control group consisting of age and education matched healthy participants. All subjects were assessed on both verb production in sentence context as well as on cognitive functions relevant for sentence processing. The verb production performances of the PD patients were correlated to their scores on executive function tasks. Analyses of PD patients' performance revealed that they have set-switching deficits and decreased sustained visual attention. The performance on verb production of PD patients was associated with the set-switching deficits, suggesting that PD patients who show poor set-switching have more difficulties with verb production. Many verb tense errors were made in sentences targeting the present tense. In our verb production task participants were instructed to inflect the verb in the past tense only in the presence of a temporal adverb referring to the past (e.g., 'yesterday') and in the present tense if the adverbial time phrase was absent. It is therefore suggested that the test materials and associated instructions provoked the tense errors. Due to the absence of a temporal adverb, PD patients were unable to switch to the present tense and showed 'stuck-in-set perseverations' which were evoked by the previous sentences. Evidence for self-monitoring deficits has earlier been reported by McNamara et al. (1992). While monitoring their performance, PD patients seemed to forget the instruction, especially in the longer subordinate sentences where working memory was challenged more than in the short main clauses. Hence, in Colman et al. (2009) set-switching impairments played a major role in performing the task assessing verb production in sentence context. These set-switching impairments reduce PD patients' performance seriously. Although the PD patients in our study did not show a decreased

working memory capacity compared to healthy speakers, verb production was associated with working memory in PD patients. In healthy speakers, the production of verbs is a rather automatic language processing task, which is confirmed by the fact that no association was found between verb production and working memory in healthy controls. Automatic behavior is thought to be mediated by the basal ganglia (Saling & Phillips, 2007). Since PD is characterized by a dopaminergic dysfunction of the basal ganglia, we assume that PD patients cannot produce verbs in a rather automatic way as well as healthy speakers and, therefore, they need to rely more on their working memory, which we consider to be a compensatory mechanism.

### 2.3 Single word production tasks

The tests of word fluency that were employed in the studies that will be discussed in the next paragraphs all test, apart from semantic memory, aspects of executive functioning. In a standard word fluency task the subjects are asked to name as many words as possible within a given semantic category (known as semantic or category fluency) or starting with a certain letter (known as phonemic or letter fluency) during a restricted time period. During an alternating fluency task, subjects have to generate words alternately using two fluency probes, which could either be from the same domain (i.e., letter-letter or category-category) or from different domains (i.e., category-letter). In a standard fluency task, planning abilities are evaluated, while in an alternative fluency task, set shifting abilities are evaluated.

Impairments in non-demented PD patients have been reported in both semantic and phonemic fluency, but the most consistent finding is impaired performance in semantic fluency (e.g., Flowers et al., 1995; Grossman, Carvell et al., 1992, Grossman et al., 1993; Gurd & Ward, 1989; Van Spaendonck et al., 1996).

Henry and Crawford (2004) did a meta-analysis of 68 studies published between 1983 and 2002 which included more than 4600 PD participants. One of the aims was to find out if the word fluency deficit associated with PD predominantly reflects executive dysfunction, or problems with semantic memory, which is related to declarative memory. The outcome of the analysis was that, although PD was associated with deficits upon tests of phonemic and semantic fluency for studies that assessed both measures, the semantic fluency deficit was significantly larger than the phonemic fluency deficit. Moreover, since the confrontation naming deficit for the Boston Naming Test (BNT; Kaplan et al., 1983), a measure that imposes only minimal demands upon cognitive speed and effortful retrieval, was equivalent in magnitude to the deficits of these two types of fluency, Henry and Crawford concluded that PD is associated with a particular deficit in semantic memory. However, tests of alternating fluency were associated with slightly larger deficits than standard measures of fluency, which supports evidence for a specific deficit in cognitive set-shifting (Henry & Crawford, 2004). Some PD patients evidenced impairments in semantic knowledge, which correlate with their executive dysfunctions (Portin et al. 2000). The exact underlying nature of the semantic deficits has yet to be determined.

Interestingly, Auriacombe et al. (1993) examined the traditional semantic and phonemic fluency tasks, but also examined fluency performance in the non-verbal modality (i.e., design fluency and category drawing task). They found that PD patients' performance on the non-verbal fluency task was comparable to healthy speakers, and confirmed the discrepancy between relatively intact phonemic fluency and impaired semantic fluency. It is not necessary to retrieve a word form during category drawing, since knowledge of the concept underlying a target superordinate (i.e., vegetable) and the exemplars that contribute



to a superordinate is sufficient. To check the hypothesis that PD patients are impaired in the retrieval of semantic information, Auriacombe et al. (1993) also administered a supraspan verbal learning task. A large proportion of the PD patients showed difficulties with free recall, but these patients were accurate at recognition, which is consistent with a retrieval deficit, and not an impairment of semantic memory itself. PD patients thus have difficulties retrieving the phonological form that is the label of an exemplar (Levelt et al., 1991).

In addition, in PD, action naming is often found to be more impaired than object naming (Bertella et al., 2002; Cotelli et al., 2007), a phenomenon also observed in agrammatic/Broca's aphasic patients. Related to this, Signorini and Volpato (2006) found that PD patients were impaired on an action fluency task but not on semantic and phonemic fluency tasks. However, analysis of spontaneous speech production of PD patients did not show the expected discrepancy between nouns and verbs, which supports the hypothesis that it is not the representation of verbs, but rather the utilization of the verb emerging under specific task demands that is troublesome (Pignatti et al., 2006). Moreover, verb fluency scores also discriminate between demented PD patients and non-demented PD patients and healthy elderly control participants, whereas tests of letter or category verbal fluency do not (Piatt et al., 1999a and 1999b). Piatt et al. (1999a, 1999b) concluded that verb fluency was particularly sensitive to the fronto-striatal pathophysiology of PD patients with dementia. According to these authors, verb fluency reflects the underlying integrity of frontal lobe circuitry, and problems on verbal fluency tasks could therefore indicate deficits in executive functioning.

Péran et al. (2003) developed a French word generation task that requires a semantic and grammar driven selection of single words over a limited time period. Compared to healthy control participants, non-demented PD patients made more grammatical errors in the noun-verb-generation task than in the verb-noun-generation task. Péran et al. (2003) suggested that this discrepancy was due to the combined effect of impaired set switching and a specific grammatical impairment in verb production. The authors assume that in the verb-noun task, the impact of impaired switching is compensated by the easier noun production, whereas in the noun-verb task both the switching and production of the verb were dysfunctional.

However, the argument that PD specifically affects verb processing was contradicted in a recent word generation study in PD conducted by Crescentini et al. (2008). Behavioral tasks already showed before that the Reaction Times (RTs) and accuracy of word generation both depend on the number of possible responses (response selection) and on the strength of association between cues and responses (associative strength) (Cheng & Martin, 2005; Martin & Cheng, 2006; Thompson-Schill & Botvinick, 2006). Based on these findings, Crescentini et al. (2008) controlled the response selection demands and association strength of the verb and the noun stimuli during a word generation task. The critical condition for PD patients was the one with a weak association between the stimulus and the response as opposed to the grammatical class. Crescentini et al. (2008) suggested that the verb generation problem in PD is caused by the fact that nouns are typically more associated with other nouns than with verbs in the semantic network. During the noun-verb condition, PD patients seem to have problems with both switching to task-relevant representations (i.e., verbs) and with inhibiting the task-irrelevant and more strongly activated options (i.e., nouns). Based on these findings, the authors proposed a non-language-specific involvement of the basal ganglia in the controlled rather than the routine semantic processes required during lexical retrieval.

One explanation for the discrepancy between verb and noun retrieval is that verb retrieval is more demanding than noun retrieval in terms of executive functioning (e.g., Péran et al., 2003; Piatt et al., 1999a and 1999b). The idea is that retrieving the name of an object elicits a more automatic lexical retrieval response than retrieval of the action name, which demands a more controlled retrieval. In other words, impaired action naming is seen as a result of executive function impairment. According to Levelt's framework (see Fig. 1), the lemmas contain information about word meaning, and word class. The lemmas of verbs additionally contain information on thematic roles, argument structure, and subcategorisation frame. Comparable to what was found for individuals with Broca's aphasia (Bastiaanse & Van Zonneveld, 2004), we suggest that for PD patients verbs are more difficult to produce than nouns, because verb lemmas contain simply more grammatical information than noun lemmas.

An alternative hypothesis for the discrepancy between verb and noun retrieval is that the link between representation of action words and representation of motor acts per se in the human motor and premotor cortex is damaged, leading to verb retrieval problems. The existence of a similar verb-naming deficit in other motor disorders, such as corticobasal degeneration (CBD) and progressive supranuclear palsy (PSP) (Cotelli et al., 2006), has provided a major argument for the idea that semantic mechanisms concerning the verb are grounded in the motor system of the brain. To test whether the motor system comes into play during the processing of verbs, Boulenger et al. (2008) compared lexical decision latencies for action verbs and concrete nouns of non-demented PD patients (off and on dopaminergic medication) using a masked priming paradigm. Priming effects for action verbs, but not for concrete nouns, were nearly absent in PD patients off treatment, confirming that processing lexico-semantic information of action words depends on the integrity of the motor system. As a follow up to their earlier French verb generation task, Péran et al. (2009) explored the relationship between the motor deficit in PD patients and brain activation in noun and verb generation tasks conducting a functional neuroimaging study. Although they did not find differences between the brain activity during the production of object-related action words and of object names, they did observe a clear relationship between brain activity and the severity of the motor deficit (as assessed by the Unified Parkinson's Disease Rating Scale (UPDRS), Fahn et al., 1987) in PD. This relation was particularly found during generation of action verbs in response to manipulable biological objects, in the pre- and post-central gyri bilaterally, left frontal operculum, left supplementary motor area and right superior temporal cortex. The impairment in the motor cortico-striato-cortical circuits in PD may result in the recruitment of a wider cortical network designed to alleviate the disturbed motor representations during the demanding generation of action verbs in response to manipulable objects.

### **3. Receptive language functions in PD**

In the following section, receptive language functions in PD, with a particular focus on sentence comprehension of non-canonical sentences, will be discussed.

#### **3.1 Comprehension of non-canonical sentences**

From the early nineties of the last century, off-line tasks such as sentence-to-picture matching and grammaticality judgment have revealed that comprehension of complex syntactic structures (i.e., non-canonical structures such as passives) is vulnerable in

individuals with PD (see Grossman, 1999 and Murray, 2008 for an extensive review). Sentences are defined as syntactically complex when the thematic roles are not in base (or canonical) word order and therefore require extra grammatical operations. The following examples are given of an active (a) and a passive (b) sentence in Dutch. Important to note is that base word order in Dutch is Subject-Object-Verb (SOV).

- a. De kinderen plukken de appels  
'The children pick the apples'
- b. De appels<sub>i</sub> worden door de kinderen t<sub>i</sub> geplukt  
'The apples are by the children picked'

In passive constructions, the *grammatical roles* are in base order. In sentence (b) the subject ('the apples') precedes the finite verb ('are') which precedes the prepositional phrase ('by the children'). However, the *thematic (semantic) roles* are not in their base position. The theme ('apples'), precedes the finite verb, whereas the agent ('children') follows the finite verb.

Lieberman et al. (1990) were among the first to find a comprehension deficit that could not be attributed to compensatory motor strategies, which had been claimed to be responsible for the sentence production deficits in PD till then (Illes et al., 1988; Illes, 1989). Lieberman et al. (1990) attributed the sentence comprehension errors in PD to "some deterioration of the patient's ability to make use of the syntactic 'rules' involved in English" (1990, p. 364). Similarly, researchers have attributed the sentence comprehension deficit to an impairment of some aspects of grammatical processing as such (Cohen et al., 1994; Natsopoulos et al., 1991, 1993). However, according to Lieberman et al. (1990), the cognitive impairments and syntactic comprehension deficits in PD have a common physiological basis; they are both caused by disruption of the cortico-striato-cortical circuits. Lieberman et al. (1990, 1992) do not regard grammatical processing and executive functions as separate mechanisms. They take the position that syntax comprehension is achieved by the operations of non-domain-specific executive functions over language-specific knowledge. Consistent with this view, some researchers claim that it is not syntax itself, but rather the interaction with executive dysfunction that might reflect the sentence comprehension deficits in PD (see for example Colman, 2011; Colman et al., 2006; Geyer & Grossman, 1994; Grossman, Carvell et al., 1992; Hochstadt et al., 2006, 2009; Kemmerer, 1999; Lieberman et al., 1990, 1992). In addition, some researchers reported deficits in lexical-semantic processing during sentence comprehension. For example, Angwin et al. (2005) reported a general semantic processing deficit, but also reported that PD patients with comprehension deficits for non-canonical sentences showed a delayed time course of semantic activation. This finding added evidence to the proposal that slowed information processing is one of the causes of the sentence processing deficits in patients with PD (Grossman, Zurif et al., 2002; Lee et al., 2003).

Grossman, Lee et al. (2002) administered both a traditional off-line sentence processing task and an on-line word detection task to the same PD patients. Subjects were instructed to press a button as soon as they heard the target word in an auditorily presented sentence. Half of the sentences contained a grammatical agreement violation (e.g., subject-verb agreement violation) prior to the target word. In healthy persons, responses to the target word were slowed down when they immediately followed a morphosyntactic error. The off-line measure of sentence comprehension required subjects to answer a simple question about a semantically unconstrained sentence. In addition to the language tasks, a battery of executive function tests was also run. Off-line, PD patients were significantly impaired on non-canonical sentences and their comprehension was correlated with the executive measures. However, PD patients and healthy control participants were equally sensitive to

violations of grammatical agreements during on-line word detection. The comprehension impairment on the traditional measure in PD was argued to be related to impairments in inhibition and planning, emphasizing the important influence of task requirements on sentence comprehension in PD.

In the same year another study by Grossman and colleagues was published, using a different on-line methodology, that is, a list priming task (Grossman, Zurif et al., 2002). Those PD patients who had problems comprehending sentences with a non-canonical structure when measured off-line (e.g., "The boy that the girl chased was friendly") showed delayed lexical retrieval during the priming task. This was reported earlier for Broca's aphasic patients (Swinney et al., 1996; Zurif et al., 1993).

The Grossman group gained additional information on the connection between slowed lexical activation and sentence comprehension deficits in PD by applying the same word detection methodology as before, but by using a different violation type. Based on previous observation of PD patients' difficulty detecting phonetic errors in grammatical morphemes (Grossman, Carvell et al., 1992), the researchers tested phonetic errors in free grammatical morphemes and words as violation type (Lee et al., 2003). PD patients were insensitive to phonetic errors in free grammatical morphemes and showed a slowed sensitivity to words located in the non-canonical sentences. This delayed sensitivity was correlated with the measure of planning, which was seen as evidence for the fundamental contribution of executive functions to sentence comprehension. Lee et al. (2003) concluded that sentence comprehension impairments are due to limitations in specific executive resources such as attention to grammatical morphemes and delayed lexical retrieval of words, rather than being a pure linguistic deficit.

Hochstadt et al. (2006) conducted the first off-line study that also tested the inter-relationship between the distinct executive functions. The authors concluded that limits on sequencing and/or verbal working memory (i.e., executive component and articulatory rehearsal) are responsible for the sentence comprehension deficits in PD. Later, Hochstadt (2009) used eye-tracking to minimize the extraneous executive demands during off-line sentence-picture matching. Some of the PD patients in this study showed difficulties comprehending passive sentences and they looked toward a distractor picture before giving a response. One of the proposed explanations by Hochstadt (2009) for the errors in passive sentences is the exaggerated agent-first bias pointing to a reliance on heuristics to compensate for impaired syntax processing. However, this explanation did not hold for passives in general, since there was no evidence that the bias differed between patients with high and low error rates in final passive trials as compared to center passive trials.

To further explore the hypothesis that executive dysfunctions are involved in the comprehension deficits of passive sentences in PD (Lieberman et al., 1992), we recently tested Dutch-speaking PD patients on the comprehension of sentences that were varied for phrase structure complexity and sentence length (Colman, 2011) to see whether there was a relation between the processing of the sentences and relevant executive function deficits. In general, the PD patients showed slightly poorer sentence comprehension compared to healthy control participants. However, the difficulties encountered by PD patients were not limited to one specific grammatical aspect. Decreased set-switching, inhibition, and working memory abilities were all associated with comprehending non-canonical passive sentences, rather than one specific executive function being primarily associated with the comprehension difficulties. Deficits in sustained visual attention appear to underlie PD patients' overall comprehension performance, possibly due to the demands of the picture-



sentence matching task. Generally, our study confirms that the language faculty is not independent from executive functioning.

Several studies using Positron Emission Tomography (PET) and functional Magnetic Resonance Imaging (fMRI) have investigated the pattern of brain activation during sentence processing in non-brain-damaged individuals. However, only a few imaging studies have investigated the underlying neural activity during sentence processing in PD patients. In an fMRI study, Grossman et al. (2003) found striatal activation in exclusively the brains of healthy senior volunteers for long sentences, relative to short sentences. Moreover, PD patients engaged significantly more brain regions associated with working memory than healthy participants to achieve the same level of comprehension accuracy as the control subjects. According to Grossman et al. (2003) the striatum contributes to cognitive resources such as working memory and information-processing speed. PD patients' sentence comprehension difficulties have been ascribed to their limited striatal recruitment, which causes an interruption of a large scale network important for cognitive resources that can interfere with sentence processing (Grossman et al., 2003).

Using Event Related Potential (ERP) studies, Friederici and colleagues have demonstrated that degeneration of the basal ganglia due to PD influences language-related ERP components dramatically and correlates with different aspects of language processing during comprehension (for an overview see Kutas & Van Petten, 1994; Osterhout & Holcomb, 1995). In a study by Kotz et al. (2002) and by Friederici et al. (2003), the PD patients included showed an intact ELAN (reflecting highly automatic first-pass parsing processes), but a strongly reduced P600. The P600 is an ERP component that is controlled by attention and is explained as indicating secondary syntactic processes such as reanalysis and repair (Friederici & Mecklinger, 1996), or as reflecting syntactic integration processes in general (Kaan et al., 2000). According to Friederici et al. (2003), the alteration in the P600 reflected distortions of the late controlled syntactic integration processes in PD. This reduction in amplitude points to a failure in the activation of the generators of this ERP component in PD patients. The reduction in PD patients' P600 amplitude points to a lack of integrity of the cortico-striato-cortical circuits responsible for the P600 generation. The patient studies by Friederici and colleagues suggest that the frontal cortex and the basal ganglia are differently involved in sentence processing or are active during different stages of auditory sentence processing. The left frontal cortex and the left anterior temporal cortex both contribute to the early automatic processing underlying the (E)LAN, whereas the left basal ganglia contribute to the late controlled syntactic integration processes underlying the P600. The difficulties with syntactic integration processes as described by Friederici et al. suggest that the language system itself is disrupted in PD patients.

In a recent fMRI study, we evaluated the patterns of activation during the comprehension of sentences in which canonicity and grammaticality were manipulated in fifteen patients with PD compared to fifteen healthy older adults (Colman, 2011). Here we focus on the activation patterns related to the processing of the passives by the PD patients and healthy control participants. Our intergroup analysis contradicted the expectation of compensatory cortical activation (Grossman et al., 2003). However, PD patients showed significant increased activation for passive versus active sentences in the left medial/superior frontal gyrus compared to healthy control participants. Three possible explanations for the activation in this frontal area during the processing of passive sentences are suggested. PD patients may rely on working memory, lexical semantics or higher-level semantic processes involved in evaluation of plausibility to compensate for the lack of activation seen in the healthy control



participants when dealing with non-canonical passive sentences. First, Carpenter et al. (1994) hypothesized that working memory load is directly related to sentence complexity. As mentioned before, higher sentence complexity is related to the non-canonical order of roles (such as in passives). All in all, non-canonical sentences impose a higher demand on working memory than canonical sentences (King & Just, 1991). The PD patients possibly relied more on their intact working memory allocated in the prefrontal cortex to compensate for their difficulties to process the non-canonical passive sentences (for a review see Wager & Smith, 2003). Secondly, examining ambiguity resolution, Stowe et al. (2004) reported a similar left medial prefrontal area as in our study, which they linked to supporting higher-level semantic processes involved in evaluation of plausibility. Finally, it is suggested that the exclusive activation of the prefrontal cortex in PD patients for passive sentences reflects a lexical-semantic strategy for dealing with word order information, which was probably not always a guarantee for successful comprehension.

### 3.2 Lexical and semantic processing

Semantic priming tasks are a straightforward measure for the evaluation of lexical and semantic processes in patients with PD. In healthy participants, RTs to the target word are faster if the prime and the target are semantically related (doctor-NURSE) as compared to when the prime and target are not related (doctor-FLOWER) (see Neely, 1991 for extensive review on priming tasks). Copland (2003) found that PD patients are unable to suppress the infrequent meaning of homophones (bank-RIVER) and proposes therefore that the selective attentional engagement of the semantic network is impaired. Thus, PD compromises the controlled aspects of semantic processing rather than the automatic processes. During sentence comprehension tasks, lexical-semantic processing has been found to be abnormal in PD patients as well (Angwin et al., 2005). Angwin et al. (2004, 2006) also found that semantic processing deficits in PD are related to striatal dopamine deficiency since automatic semantic activation was compromised in PD patients when off medication.

Spicer et al. (1994) were the first to evidence a unique increased semantic priming effect in PD patients as compared to the normal control subjects, which they called 'hyperpriming'. This hyperpriming was suggested to be caused by slowness in the unrelated prime-target conditions. Spicer et al. (1994) suggested two possible levels of the deficit, either the pre-lexical level or the post-lexical level. Somewhat later, the same research group (McDonald et al., 1996) revised their theory and concluded that PD patients show poor performance whenever the task requires switching between response sets or different semantic categories. However, rather than hyperpriming reflecting a switching problem between semantically unrelated words, Mari-Beffa et al. (2005) suggested that a lack of lexical-semantic inhibitory control in participants with PD is responsible for it. This idea was confirmed by Castner et al. (2007), who furthermore concluded that subthalamic nucleus stimulation restored these inhibitory processes. Consequently, it is concluded that the basal ganglia are involved in both the automatic and controlled aspects of semantic priming and thus support both the involved facilitation and inhibition processes.

### 3.3 Verb processing

Using receptive tasks, the existence of a specific verb processing deficit in PD was found. Grossman et al. (1994) reported impaired verb learning. They taught PD patients and healthy age-matched controls the grammatical and semantic information of a new verb ('to wamble'). The semantic and grammatical information of the new verb was probed by sentence judgment

and picture classification. Significant impairment in recalling some aspects of the new verb was seen in 55% of the PD patients. These patients demonstrated a language-sensitive deficit in “appreciating grammatical information represented in the new verb” (Grossman et al., 1994, p. 413). However, a small number of PD patients responded randomly to probes of all information about the new verb, which suggests a memory impairment in these patients. More recently, Whiting et al. (2005) evaluated verb and context processing in PD by using a self-paced stop making sense task. The participants had to pace themselves through a sentence that was preceded by a context, which made the thematic role of the verb plausible or implausible. They found that PD patients were impaired in thematic role mapping, which was consistent with previous findings of Geyer and Grossman from 1994. Whiting et al. (2005) proposed that PD participants in their study processed sentences “on a more superficial level” than control subjects and concluded that the PD patients’ performance was caused by both global discourse comprehension difficulties and impaired working memory.

### **3.4 Perceptive pragmatic language abilities**

In daily life, healthy individuals interpret the intended meaning of language appropriate to the social context. Another line of research in receptive language functions has been focusing on the pragmatic language skills of PD patients. Pragmatic language use entails the ability to interpret nonliteral elements of language such as metaphors, proverbs, idioms, etc. Berg et al. (2003) conducted a survey of pragmatic language abilities and reported that PD patients exhibit impairments in making inferences, comprehending metaphors and lexical ambiguities. The study by Whiting et al. (2005) showed that PD patients were less accurate than the control participants in using previously encountered discourse antecedents when deciding that a sentence stopped making sense. This is in line with the finding of Grossman, Crino et al. (1992) in which PD participants displayed an impaired ability to answer questions about previously encountered discourse elements compared to control participants. In addition, patients with PD have these problems also when resolving lexical ambiguities (Copland et al., 2001).

Monetta and Pell (2007) investigated how PD patients process metaphors using a timed property verification task (by Gernsbacher et al., 2001) compared to healthy control participants. The impact of PD on metaphor comprehension varied as a function of working memory ability, meaning that PD patients with a reduced working memory capacity were impaired in the comprehension of metaphors, whereas PD participants at a similar stage of disease but without working memory difficulties performed as good as the healthy control participants (Monetta & Pell, 2007). In a follow-up, similar results were found for inference generation (Monetta et al., 2008) and irony comprehension (Monetta et al., 2009). McKinlay et al. (2009) related pragmatic language skills to cognitive functions and suggested that processing speed was a stronger determiner of pragmatic language performance than working memory.

Research relating the pragmatic language problems of PD to their executive function deficits might be influenced by the research investigating morphosyntactic processes during sentence comprehension in PD patients.

## **4. Impact of language processing deficits on the daily life of PD patients**

The subtle deficits in language comprehension and production in PD will lead to communication problems that may result in decreased socialization and participation in

society. Miller et al. (2006) investigated the impact of particularly 'speech and voice' deficits on the life of the individual with PD and their family. To this purpose, a group of PD patients was interviewed to explore the onset of speech changes, their impact and patients' strategies to manage these changes. In general, the changes in PD patients' speech and voice had an effect on the overall communication, roles and relationships of those confronted with the disease. It was shown that alterations in speech do not need to be severe to have a significant impact. However, in addition to the speech and voice problems some of the interviewees reported difficulties with word retrieval, sentence formulation and comprehension. This suggests the necessity to refer all newly diagnosed PD patients to speech and language therapy. According to us, this preventive therapy will not only serve articulation and intelligibility abilities, but should also focus on the assessment and remediation of language problems. From our review it is clear that some PD patients suffer from unawareness of the extent of their communicative problems. During social conversations, deficit in the monitoring system influenced turn taking abilities and topic maintenance (McNamara et al., 2003). This unawareness or self-monitoring deficit can prevent the development of adaptive coping strategies, provokes feelings of frustration and might lead to complete withdrawal from communication. PD patients can profit from insights in their language disorders, for example it can help them to use effective compensation strategies or to simply inform the other speech partner of the impact of their disease on communication. From our clinical experience it is clear that patients and their caregivers are often surprised to hear that not only motor symptoms, but also language processing can be affected in the course of the disease. This review on language problems in PD may help in bringing the topic under the attention of those confronted with the disease, meaning that professionals need more up-to-date information. Up-to-date knowledge on the language problems on the part of the patients' environment will facilitate successful communication and, thus, support good family relations. Hence, including routine screening for cognitive decline and language problems early in the disease, in addition to supplying information on PD patients' language problems to caregivers and professionals could keep the PD patients from becoming socially isolated. Examples of communication advice for caregivers could be to simplify and avoid redundancy of information. Speech and language therapy must provide information in tune with the patient's individual limitations and wishes towards language and speech, which in turn can facilitate patients and their environment to implement coping strategies when communicative contexts are arising. In addition, we expect that intensive training of cognitive functions and strategies in PD patients will positively influence processing in the language domain. In the near future a therapy effectiveness study will be developed, which will remediate language problems in combination with executive function deficits in PD.

## 5. Suggestions for future research

Medication with levodopa is well known to improve the motor symptoms. However, the effects on cognitive functions are more complex: both positive as well as negative effects have been observed. According to Cools (2006), these contrasting effects of levodopa are due to the spatio-temporal progression of dopamine (DA) depletion in PD. PD starts in the dorsal striatum (tail of the Caudate nucleus) and progresses to the ventral striatum (head of the Caudate nucleus). Levodopa in early stages of the disease may improve cognitive functions of the dorsal striatum while simultaneously 'over-dosing' functions of the ventral

striatum. This effect of over-dosing is related to the base level of DA in underlying cortico-striato-cortical circuitry and the task instructions. Therefore, in future research, to control for the influence of dopaminergic medication on cognitive processing, we suggest conducting experiments in the practically defined 'off state'. This is typically following an overnight fast from the patient's anti-Parkinson medications. More positive results are expected in this 'off state', but we also expect more influence of other factors such as frustrations with task performance and tremors and rigidity making testing in the MRI scanner impossible. Ultimately, conducting experiments in drug naïve 'de novo' patients is preferred, but clinically these patients are not always willing to participate in research. Apart from the important effects of medication on language processing, the variables of disease duration and age of onset of PD should be taken in consideration in future research.

Future studies on the influence of set-shifting and working memory on sentence processing in PD can benefit from the use of better-controlled and better-understood methods than the clinical accepted neuropsychological tests which were used in the studies reported above. For example, reading span tasks have been used as tests of working memory because they require active manipulation of information and concurrent item retention (Just & Carpenter, 1992). However, reading span tasks rely on many of the same processes as reading comprehension tasks (Engle et al., 1992), which makes it difficult to draw any strong conclusions in terms of the mediating value of working memory for exactly that language process.

In the near future, the nature of the connectivity between the inferior frontal gyrus and the basal ganglia can be further explored. A functional connectivity analysis can provide functional evidence for a basal ganglia-frontal cortical network during the comprehension of sentences in which the variables of canonicity and grammaticality are crossed. However, it is generally known that in fMRI, temporal resolution is inferior and that it cannot index neural activity that is specifically time-locked to the critical word itself. The temporal coarseness of the fMRI method probably blurred the linguistic processes. Simultaneous ERP/fMRI may allow improved localization of neural generators as well as enhanced temporal resolution of BOLD activation foci. Functional connectivity analysis can be used to examine the degree of collaboration between language-specific cortical areas and the basal ganglia, when processing violated compared to non-violated sentences. In on-line behavioral tasks, the impact of executive functions necessary for syntactic processes per se and the executive functions necessary for the task can potentially be disentangled. Therefore, a valuable technique for obtaining on-line data from sentence-picture matching is the eye-tracking method as suggested by Hochstadt (2009).

Finally, as evidenced by this review, there exists an extensive amount of literature on language processing in PD, but language processing in other motor syndromes has received little attention. The existence of a similar verb naming deficit in other movement disorders, such as CBD and PSP (Cotelli et al., 2006) has provided a major argument for the theory that semantic characteristics of the verb are grounded in the motor system of the brain. It will be interesting to test verb production related to cognitive functions in the following movement disorders:

Multiple system atrophy (MSA) is an adult-onset, sporadic, progressive neurodegenerative disease characterized by varying severity of Parkinsonian features, cerebellar ataxia, autonomic failure, urogenital dysfunction, and corticospinal disorders (Gilman et al., 2008). MSA is also accompanied by cognitive impairments associated with dysfunctional cortico-striato-cortical circuits (Herting et al., 2007).



PSP is a neurodegenerative disease characterized by defects in the vertical ocular gaze, bulbar dysfunction, increased frequency of falling, and akinetic-rigid features. In addition, cognitive impairments, in particular executive dysfunctions associated with alterations within the frontostriatal circuitry, occur (Millar et al., 2006).

CBD is characterized by slowly progressing, unilateral Parkinsonism with dystonia or myoclonus, unresponsiveness to Levodopa, and limb apraxia. Patients with CBD often demonstrate impairments in visuospatial processing and visuoconstruction (Tang-Wai et al., 2003) in combination with acalculia, dysexecutive symptoms and aphasia (McMonagle et al., 2006).

Thus far, only a few studies have investigated language processing in patients with atypical Parkinson syndromes, such as MSA (Apostolova et al., 2006), PSP and CBD (Josephs & Duffy, 2008; McMonagle et al., 2006).

## 6. Conclusion

This review highlights that the progressive degeneration of the cortico-striato-cortical circuits due to PD disturbs executive functioning and, thus contributes to deficits in language production and comprehension. One of the major conclusions based on this review is the importance of evaluating both the executive functions and modalities of language processing (i.e., comprehension and production) in patients with PD. This is not only crucial for our understanding of PD and for the relationship between languages and executive functions, but it is also particularly useful for efficiently identifying the needs for direct intervention

More research still needs to be done to illuminate further the impact of PD on language processing. Future research needs focus on the clinical implementation of evidence-based communication guidelines in order to guarantee a better quality of life for patients suffering from PD.

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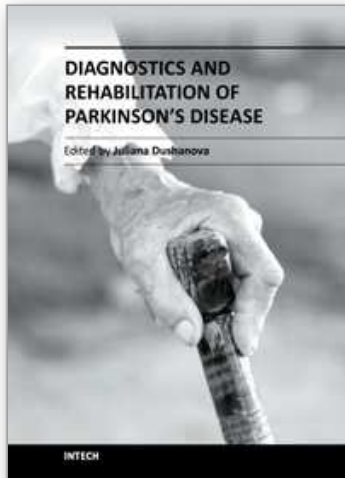


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## **Diagnostics and Rehabilitation of Parkinson's Disease**

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Diagnostics and Rehabilitation of Parkinson's Disease presents the most current information pertaining to news-making topics relating to this disease, including etiology, early biomarkers for the diagnostics, novel methods to evaluate symptoms, research, multidisciplinary rehabilitation, new applications of brain imaging and invasive methods to the study of Parkinson's disease. Researchers have only recently begun to focus on the non-motor symptoms of Parkinson's disease, which are poorly recognized and inadequately treated by clinicians. The non-motor symptoms of Parkinson's disease have a significant impact on patient quality of life and mortality and include cognitive impairments, autonomic, gastrointestinal, and sensory symptoms. In-depth discussion of the use of imaging tools to study disease mechanisms is also provided, with emphasis on the abnormal network organization in parkinsonism. Deep brain stimulation management is a paradigm-shifting therapy for Parkinson's disease, essential tremor, and dystonia. In the recent years, new approaches of early diagnostics, training programmes and treatments have vastly improved the lives of people with Parkinson's disease, substantially reducing symptoms and significantly delaying disability. Written by leading scientists on movement and neurological disorders, this comprehensive book should appeal to a multidisciplinary audience and help people cope with medical, emotional, and practical challenges.

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