Behavioral and neuroimaging studies on language processing in Dutch speakers with Parkinson's disease
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Chapter 3
Role of the basal ganglia in language processing

3.1 Introduction

Right from the start of the discipline aphasiology, the role of the basal ganglia (BG) in language has been debated (Broadbent, 1872; Kussmaul, 1877; Marie, 1906; Wernicke, 1874). Some authors (e.g. Alexander, Naeser, & Palumbo, 1987; Nadeau & Crosson, 1997) have suggested that the BG are not directly involved in language processing. For example, Nadeau and Crosson (1997) proposed that cortical hypoperfusion, following striato-capsular infarction, may be the crucial factor for language impairments after subcortical damage (see for detailed discussion Crosson, Benjamin, & Levy, 2007). The fundamental concepts of Nadeau and Crosson (1997) were recently also further corroborated by the cerebral perfusion studies conducted by Hillis and her colleagues in patients with subcortical lesions (Hillis, et al., 2002). However, researchers from various disciplines, ranging from robotics to neuropsychology, suggested models for processes mediated by the BG and their interactions with other areas of the brain (Beiser et al., 1997; Bergman et al., 1998; Alexander et al., 1986) and aimed at resolving the conundrum of the role of the BG in language. Studying linguistic symptoms resulting from neurodegenerative diseases such as Parkinson’s disease (PD) will give us more insights into the functions of the BG in language processing.

Before elaborating on PD patients’ impairments in production and comprehension, a psycholinguistic framework by Levelt (1983, 1989) will be introduced that brings together automatic and controlled processing parts of both speech production and comprehension. In the subsequent sections, we will first elaborate on the similarities and differences in language deficits between PD and Broca’s aphasia in order to better understand the common neurophysiological basis of the impairments, namely specific lesions of the cortico-striato-cortical circuits. The next section will deal with hypotheses on the role of the BG in morphosyntactic processing. This chapter on the role of the BG in language processing will be concluded by presenting our own research questions.

3.2 Levelt's model on sentence production and comprehension

The experiments described in this thesis examined production and comprehension of syntactic structures by PD patients. Levelt’s framework for sentence processing (1983, 1989) clarifies both production and comprehension of spoken language and implements the distinction between controlled and automatic processing. Figure 3.1 proposes Levelt’s “Blueprint for the speaker” and shows the architecture of the various processes involved in speech production and comprehension.
Within this framework the boxes represent processing components and the circle and 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 he intends to communicate in the Conceptualizer. Conceptualizing demands working memory (WM) (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 of the Formulator must access lemma information 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 (NPs)], specifying the hierarchical relation between syntactic constituents and their linear order. In a second step, the Phonological Encoding component of the Formulator uses the sentence representation to construct 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 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 Figure 3.1, 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 speech in terms of phonological, morphological, syntactic, and semantic composition. This representation is further processed by the Conceptualizer. Sentence parsing during comprehension is constrained by WM 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 Figure 3.1). 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’). Speakers then use the Audition component to analyze their own speech. Both of the 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 is described as being a central, conscious process that oversees end products of speech production (Postma, 2000). This description of the Monitoring process during production appears to be very similar to the monitor of the ‘supervisory attentional system’ (SAS). The monitor of the SAS screens ongoing behavior and receives emotional and/or motivational information (see Figure 2.6 in Chapter 2, p. 19). Thus, the SAS monitors the processes by which action schemas are routinely selected, and intervenes when these contention-scheduling processes are inadequate.


In contrast to error detection during production, during perception a comparison between intentions and actual events (Levelt 1983, 1989) is not possible. However, individuals can have expectations about what the other person (speaker or writer) intended. There is evidence for prediction during spoken and written language comprehension. Linguistic context predicts upcoming words in sentences. For example, ‘syntactic prediction’, involves the prediction of constituents from the syntactic structure already built (Gibson, 1998). A conflict between a highly expected representation and an unexpected representation might trigger a monitoring process and a reanalysis of the sentence to check the input for processing errors. The conflict between the different representations (i.e., heuristics and syntactic rules) “constitutes the internal signal to detect errors of language perception” (Van
de Meerendonk et al., 2009, p. 1213). As will be discussed in more detail in Chapter 6, modulation of the P600 effect reflects the process of reanalysis of the linguistic input. Furthermore, violations of non-linguistic abstract structures have also been found to elicit a P600-like positivity (Lelekov-Boissard & Dominey, 2002).

In his review on BG functions, Saint-Cyr (2003) stated that while consciously selected goals, awareness of the environment and identification of salient cues by the SAS must be attributed to the cortex, context may be implicitly encoded by the BG. The context recognized by the cortex may be the cue used by the BG to evoke dopamine-potentiated, but cortically-determined, rules (Wise et al., 1996). After the input structures of the BG (i.e., striatum) detected cortically recognized contexts, simultaneous transmission through the direct and indirect pathways leads to the selection of activation patterns in the output structures. These activation patterns eventually serve to facilitate processing routines in the frontal cortex that have been rewarding in similar contexts before.

From the literature it is clear that PD disrupts the processes involved in both language production and comprehension. In PD, even at the pre-articulatory, abstract linguistic level, impairments in production have been reported. Furthermore, PD patients are known to have impaired comprehension of complex syntactic structures (see Grossman, 1999 and Murray, 2008 for an extensive review). The finding of a deficit in both sentence production and comprehension in PD argues against the idea of adaptation to their motor deficits as a compensatory strategy. To document the dysfunctions in language production and comprehension in PD, the literature on language research in PD is reviewed in the following section. This review will not be limited to the deficits at the sentence level, which can be explained by impairments in subparts of Levelt’s framework, but will also consider deficits at the word and discourse level.

### 3.3 Language functions in patients with Parkinson’s disease

#### 3.3.1 Language production

*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, Hohenstein, Poewe, & Butterworth, 2000). Also, their prosody, facial expression and gestures are abnormal, probably because these are influenced by the cardinal motor impairment.

Grammatical effects in the spontaneous speech of PD patients 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. However, 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.

McNamara, Obler, Au, Durso, and Albert (1992) suggested that in PD a reduced capacity to simultaneously speak and monitor one’s own speech is responsible for PD patients’ self-monitoring impairments. To test overt speech monitoring in narrative discourse of patients with PD, they used the Cookie Theft picture 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 non-brain-damaged subjects (NBDS) and used both repair strategies, but relatively less often than the NBDS: patients with PD only corrected 25% of their errors. According to the authors this speech monitoring impairment is related to attentional dysfunction in PD. They furthermore suggest that PD patients display reduced sensitivity to context, which might complicate their language comprehension. Reduced capacity to simultaneously speak and monitor one’s own speech could also account for the self-monitoring impairments found in Broca’s aphasia (Oomen, Postma, & Kolk, 2005). More recently, Ellis (2006, see also Ellis & Rosenbek, 2007) analyzed narrative discourse in individuals with PD compared to healthy control (HC) subjects. They concluded that patients with mild to moderate PD demonstrate deficits in language use while maintaining spared language form.

In order to evaluate PD patients’ pragmatic skills, McNamara and Durso (2003) used a formal pragmatic communication skills protocol (Prutting & Kirchner, 1987). The pragmatic communication deficits 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 less aware of their communication problems.

In line with Levelt’s framework (1989, see Figure 3.1) it is concluded that PD patients do not detect errors or the mismatch in comparing their intentions and the actual output.

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10 Pragmatic skills involve the ability to use and interpret verbal and nonverbal language appropriately within the social context in which the communicative exchange occurs, requiring a degree of inference and interpretation (Perkins, 2005).
**Verb production in sentence context**

In 1997, Ullman and colleagues obtained evidence for a role of the BG in morphosyntactic production. Ullman et al. (1997) reported on 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 BG system, which is damaged in PD, constitutes the procedural memory system that regulates grammar (grammatical encoder in Figure 3.1) and that the mental lexicon depends on declarative memory (see Figure 3.1), embedded in the temporal lobe, which is largely intact in PD. Set in Levelt’s framework (Figure 3.1), it is proposed that PD patients have a deficit in an aspect of 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, Tyler, Marslen-Wilson, 2003, Longworth, Keenan, Barker, Marslen-Wilson, & Tyler, 2005; Penke, Janssen, Indefrey, & Seitz, 2005; Terzi, Papapetropoulos, & Kouvelas, 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). As an alternative explanation, and as illustrated in the Figures 2.6 and 3.1, we suggest that inhibition of the response occurs after activation of the monitor, possibly upon detection of an error, and after which a reanalysis/repair process starts (see also Figure 3.1, Levelt, 1983, 1989). It is therefore suggested that during production, because of a failing monitor and subsequent disturbed inhibition process, PD patients are not able to repair errors in their output.

**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, in addition to the intactness of semantic memory, aspects of executive functioning (see Figure 2.6, p. 19). For example, planning abilities are evaluated by a standard word fluency task, while set shifting abilities are evaluated with the alternating fluency task. 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.
Impairments in either semantic or phonemic fluency tasks in non-demented PD patients have been reported in the literature, but the most consistent finding is impaired performance in semantic fluency (e.g., Flowers, Robertson & Sheridan, 1996; Grossman, Carvell, Stern, Gollomp, & Hurtig, 1992a, Grossman et al., 1993; Gurd & Ward, 1989; Van Spaendonck, Berger, Horstink, Buytenhuijs, & Cools, 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 BDAE (Goodglass & Kaplan, 1972), 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).

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 HC subjects, 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 (Levett 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, in an analysis of spontaneous speech production 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 (Pignatti et al., 2006). Moreover, verb fluency scores also seem to discriminate between demented PD patients and non-demented PD and healthy

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11 Cognitive speed stands for how fast we can think.

12 See Appendix C for a brief description of the verb or action fluency task as designed by Piatt et al., 1999a, 1999b and 2004.
elderly control subjects, 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 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 HC subjects, 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) hypothesized that this discrepancy was due to the combined effect of impaired set switching and a specific grammatical impairment in verb production. The authors suggested 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, Mondolo, Biasutti and Shallice (2008). Behavioral tasks showed already that the Reaction Times (RTs) and accuracy of word generation depend both 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 more strongly activated options (i.e., nouns). Based on these findings, the authors proposed a non-language-specific involvement of the BG in the SAS rather than the routine semantic processes required during lexical retrieval (see Chapter 2, Figure 2.6, p. 19).

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.

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 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. In a neuro-imaging follow-up study 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. 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 (UPDRS) scale, 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.

3.3.2 Language comprehension

Lieberman, Friedman and Feldman (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 (Illes et al., 1988; Illes, 1989). In the following, receptive language functions in PD will be discussed.

Comprehension of non-canonical sentences

From the early nineties, off-line tasks such as sentence-to-picture matching and grammaticality judgment have revealed that complex syntactic structures (i.e., non-canonical structures such as passives; sentences with center embedded clauses) are most vulnerable in individuals with PD (see Grossman, 1999 and Murray, 2008 for an extensive review). Over the years, similar sentence comprehension deficits were found in several independent studies using different off- and on-line methodologies and sentence materials (see Chapter 5 and Cohen, Bouchard, Scherzer, & Whitaker, 1994; Colman, Koerts, Van Beilen, Leenders & Bastiaanse, 2006; Grossman, 1999; Grossman et al., 1991, 1992a, Grossman, Crino, Reivich, Stern, & Hurtig, 1992b, Grossman et al., 1993, 2000, 2001, Grossman, Lee, Morris, Stern, & Hurtig, 2002a, Grossman et al., 2002b; Hochstadt, 2009; Hochstadt, Nakano, Lieberman, & Friedman, 2006; Kemmerer, 1999; Lee et al., 2003; Lieberman et al., 1990, 1992; Natsopoulos et al., 1991, 1993; Skeel et al., 2001).

Most relevant to the research described in this thesis are PD patients’ impairments in the comprehension of passive sentences (Lieberman et al., 1992). Sentences are defined as syntactically complex when the thematic roles are not in basic (or canonical) word order and therefore require extra grammatical operations. As already explained in Chapter 1 of this thesis, in passive sentences the grammatical roles are in base position (S-Vin⁰-PP-V), while the thematic roles are in derived position (i.e., the theme is preceding the agent). Terzi et al. (2005) investigated in Greek speaking PD patients the comprehension of two types of
passive sentences (verbal and adjectival) compared to active sentences. They found a significant difference between adjectival passives and actives in PD and suggested that this was because the adjectival passive is less natural in contexts in which the agent is expressed in the by-phrase. Problems with the passives in PD were also described when comprehension of the passive voice was complicated by additional factors such as length in combination with matching of the sentence and the picture (Chapter 5 of this thesis), when real-world knowledge could not be used to understand the sentence (Hochstadt et al., 2006) or when the passive sentences contained a center-embedded relative clause rather than a final relative clause (Hochstadt et al., 2006).

A review of the literature shows no consent concerning the underlying impairment. Some 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). Others have provided evidence for a significant relation between executive dysfunction and sentence comprehension difficulties in PD (see Chapter 5 and Colman et al., 2006; Geyer & Grossman, 1994; Grossman, Carvell et al., 1992a; Hochstadt et al., 2006; Kemmerer, 1999; Lieberman et al., 1990, 1992). 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. As Lieberman et al. (1992) stated:

“The cognitive and syntactic comprehension deficits that occur in PD, . . . , appear to have a common physiologic basis—the disruption of neural circuits to prefrontal cortex. Thus it makes little sense to attribute human syntactic ability to an “encapsulated module” of the brain, i.e., a neural system that operates only in the domain of syntax. Nor can the neural domain of the module be restricted to cortical structures. The syntax module can, of course, be restricted to the mechanisms by which a person’s knowledge of the syntactic rules of his/her language is encoded, but syntactic ability will deteriorate if these rules cannot be accessed or applied” (1992, p. 186).

Hochstadt et al. (2006) conducted the first off-line study that, in addition to looking at the relation between sentence comprehension and executive functions, also tested the interrelationship between the distinct executive functions. The authors concluded that limits on sequencing and/or verbal WM (i.e., executive component and articulatory rehearsal) may be responsible for the sentence comprehension deficits in PD. Somewhat 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. These patients initially looked toward a picture of a sentence with a verb distracter, which portrayed the subject NP as the ‘agent’, which is the reversed of its thematic role, the ‘theme’. One of the proposed explanations by Hochstadt (2009) for the errors in passive sentences is the exaggerated agent-first bias pointing to an exaggerated 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.
Grossman, et al. (2002a) 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 controls, response to the target word was slowed down when it immediately followed a morphosyntactic error. The off-line measure of sentence comprehension required subjects to answer a simple question about a semantically unconstrained sentence with a grammatical structure that has a final or center embedded subordinate clause. Half of the subordinate clauses were canonical (e.g., “The whale pursued the dolphin that surprised the shark”), while the other half was non-canonical (e.g., “The zebra hunted the fox that the elephant scared”). In addition to the language tasks, a battery of executive function tests was also run: a semantic fluency task, the Stroop test, the Trail Making Test Part B and the digit span test (see Appendix C for details on the tests). Off-line, PD patients were significantly impaired on non-canonical sentences and their comprehension was correlated with the executive measures. However, PD patients and HC subjects were just as 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 the Grossman group was published, using a different on-line methodology, that is, a list priming task (Grossman, et al., 2002b). PD patients having off-line problems comprehending sentences with a non-canonical structure (e.g., “The boy that the girl chased was friendly”) showed slowed lexical retrieval during the priming task, which is comparable to what was found earlier for Broca’s aphasis patients (Swinney, Zurif, Prather, & Love, 1996; Zurif, Swinney, Prather, Solomon, & Bushell, 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 et al., 1992), the researchers chose phonetic errors in unbound grammatical morphemes and words as violation type (Lee, Grossman et al., 2003). PD patients were insensitive to phonetic errors in unbound grammatical morphemes and showed a slowed sensitivity to words located in the non-canonical sentences. This delayed sensitivity was furthermore correlated with the measure of planning, which was seen as evidence for the fundamental contribution of executive functions to sentence comprehension. It was concluded that sentence comprehension impairments are due to limitations in specific executive resources such as attention to grammatical morphemes and slowed lexical retrieval of words, rather than being a pure linguistic deficit.

However, another possibility is that the impaired processing of non-canonical sentences, in which thematic roles based on word order (heuristic strategy) conflict with those generated syntactically, is also consistent with a deficit in the monitoring process during comprehension, as described by Kuperberg (2007), Van de Meerendonk, Kolk, Chwilla and Vissers (2009), Van Herten (2006), Van Herten, Chwilla and Kolk (2006) and Vissers (2008).
**Semantic priming**

As indirectly suggested above, semantic priming tasks are a straightforward measure for the evaluation of the automatic and controlled processes by which individuals activate information stored in semantic memory. Automatic spreading activation is fast, occurs unconsciously and results in faster RTs in related prime-target conditions relative to a baseline condition. Controlled processing is slower, requires attention and can result in slower RTs in unrelated prime-target conditions relative to a baseline condition (Neely, 1977; Posner & Snyder, 1975).

Copland (2003) found that PD patients are unable to suppress the infrequent meaning of homophones and proposes therefore that the selective attentional engagement of the semantic network is impaired. Thus, PD compromises controlled aspects of semantic processing rather than the automatic processes (Arnott, Chenery, Murdoch, & Silburn, 2001; Copland, 2003; Copland, Chenery, & Murdoch, 2000). According to these authors there is no pure linguistic deficit in PD. However, other semantic priming studies suggest that PD also causes changes in the automatic access of semantic information (Angwin, Chenery, Copland, Murdoch, & Silburn, 2004, 2005, 2007). For example, Angwin et al. (2005) reported a general semantic processing deficit, but also mentioned 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 may contribute to the sentence processing deficits in patients with PD (Lee et al., 2003) or with Broca’s aphasia (Swinney et al., 1996; Zurif et al., 1993). In another line of research, Angwin et al. (2004, 2006) 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 (Angwin et al., 2004, 2006).

Remarkably, Spicer, Brown and Gorell (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 theories, either based on a pre-lexical deficit or a post-lexical deficit. Somewhat later, the same research group (McDonald, Brown, & Gorell, 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 cost between semantically unrelated words, Mari-Beffa, Hayes, Machado, & Hindle (2005) suggested that a lack of lexical-semantic inhibitory control in participants with PD is responsible for it. This finding was confirmed by Castner er al. (2007), who furthermore concluded that subthalamic nucleus stimulation restored these inhibitory processes.

It might thus by concluded that the BG are involved in both the automatic and controlled aspects of semantic priming and thus support both the involved facilitation and inhibition processes.
Verb processing

Using receptive tasks, the existence of a specific verb processing deficit in PD was affirmed. Grossman, Stern, Gollomp and Vernon (1994) found impaired verb learning. They taught PD patients and age-matched controls the grammatical and semantic information of a new verb. 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 word, which suggests memory impairment in some of the patients. More recently, Whiting, Copland and Angwin (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 WM.

Perceptive pragmatic language abilities

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. Related to this result is the finding of the study by Grossman et al. (1992b) 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 difficulty integrating previously encountered discourse elements when resolving lexical ambiguities (Copland, Chenery, & Murdoch, 2001).

Pragmatic language use entails furthermore the ability to interpret nonliteral elements of language such as metaphors, proverbs, idioms, etc. PD patients have shown to be impaired in the comprehension of metaphors. In addition to measures of language production, Berg, Bjornram, Hartelius, Laakso and Johnels (2003) reported that PD patients exhibit impairments in making inferences and comprehending metaphors. Monetta and Pell (2007) investigated how PD patients process metaphors using a timed property verification task (by Gernsbacher, Keysar, Robertson, & Werner, 2001) compared to healthy control subjects. They found that the impact of PD on metaphor comprehension varies as a function of WM abilities, meaning that PD patients with a reduced WM capacity were impaired in the comprehension of metaphors, whereas PD participants at a similar stage of disease but without WM difficulties performed as good as the healthy control subjects (Monetta & Pell, 2007). Mc Kinlay, Dalrymple-Alford, Grace and Roger (2009) also related pragmatic language skills to cognitive functions and suggested that processing speed was a stronger determiner of pragmatic language performance than WM.
3.4 Language deficits in Parkinson’s disease and Broca’s aphasia: overlap?

In order to better understand the contribution of the distinct parts of the cortico-striato-cortical circuits (i.e., frontal areas and BG) to language processing, we will report in this section on the results of studies clarifying the similarities and differences between the language deficits in PD and Broca’s aphasia. Lieberman et al. (1992) suggested that similarities in language deficits between PD and Broca’s aphasia have a common neurophysiologic basis, namely lesions of the cortico-striato-cortical circuits. It is well known that damage to the BG due to stroke may result in aphasia. Crosson (2008) found that the size of the BG lesion was negatively correlated to post-lesion improvement in both action naming and object naming. Thus, the bigger the BG lesion, the worse treatment results. This finding is consistent with the finding of Brunner et al. (1982) that patients with left unilateral BG in combination with cortical damage show more persistent aphasias than patients with isolated cortical lesions. The question remains whether a lesion of the BG alone will lead to the similar language deficits seen in PD patients. In the following paragraph, we will first give a brief summary of the classical description of Broca’s aphasia.

Traditionally, Broca’s aphasia was thought to be restricted to speech production. Oral production in Broca’s aphasia is characterized by ‘telegraphic’ or ‘agrammatic’ speech, in which bound and free grammatical morphemes are often omitted and/or substituted, and is combined with articulatory disturbances. Several competitive accounts tried to explain the underlying deficit of the (complete or partial) loss of functional elements in agrammatic speech production: some phonological (Kean, 1977, 1979), some lexical (e.g., Bradley, Garrett, & Zurif, 1980), and some syntactic (e.g., Caplan, 1983). Kolk’s (1995) adaptation theory locates the source of agrammatic production in the Grammatical Encoder, leading to problems in building up a sentence representation, while the self-monitoring system is largely intact (see Figure 3.1). Consequently, the large number of disfluencies in Broca’s aphasic patients spontaneous speech might reflect attempts to restart disintegrated sentence representations detected by the internal monitoring loop (Kolk, 1995).

In short, a variety of theoretical accounts has been proposed concerning the sources of the production problems in Broca’s aphasia, but most aphasiologists agree that a grammatical deficit underlies the phenomenon (Bastiaanse & Edwards, 2004).

This initial focus on the production of Broca’s aphasia was adjusted in the 1970s when controlled experiments on sentence comprehension began. Caramazza and Zurif (1976) showed in their pioneering work that the performance of Broca’s aphasics subjects dropped from near normal to chance performance when the canonical subject-verb-object (SVO) order of semantically reversible sentences was altered into a non-canonical object-verb-subject (OVS) order. Since then, this observation has been replicated in several languages (e.g., Bastiaanse & Edwards, 2004 for Dutch and Burchert, Meißner, & De Bleser, 2008 for German). Agrammatic individuals also have difficulty in understanding sentences with complex verb-argument-structure properties or those with more than one verb (Caplan, Baker, & Dehaut, 1985; Caplan & Hildebrandt, 1988; Caramazza & Zurif, 1976; Nespoulous et al., 1988; Schwartz, Saffran, & Marin, 1980).
As discussed in the previous section, similar grammatical deficit has also been reported in PD. Lieberman (2000, 2006) thoroughly discussed evidence that links the language problems evident in Broca’s aphasia and PD. However, McNamara, Krueger, O’Quin, Clark and Durso (1996) compared directly the grammatical judgments and the comprehension ability of a group of English speaking non-demented PD patients to that of a group of Broca’s aphasic patients. They concluded that the pattern of language impairment in PD patients differed “dramatically” from that of the patients with Broca’s aphasia. Both in the grammatical judgment task and the comprehension task, PD patients scored consistently and significantly better than patients with Broca’s aphasia, except when ‘off’ medication. Colman (2003) compared Dutch-speaking, non-demented PD patients and Broca’s aphasic patients. Tasks that addressed two grammatical aspects of comprehension and production were presented to both patient groups. First the influence of word order on comprehension and construction of sentences was examined. Secondly, the study addressed inflection for tense and agreement in verb production. It was expected that if a linguistic dysfunction is associated with PD, PD patient’s performance should show the same pattern as in Broca’s aphasia, although maybe less severely, depending on the progression of the illness. In correspondence with the finding of McNamara et al. (1996), PD patients on their medication did not evidence a similar linguistic dysfunction relative to Broca’s aphasic patients.

Although the studies described above suggest both overlap and differences of language impairment between Broca’s aphasia and PD patients, a closer look in the bulk of studies in both patient groups taken separately supports a related functional neurological basis for the language deficits in both groups.

First, studies in PD have revealed specific deficits in the processing of verbs (e.g., Bertella et al., 2002, Boulenger et al., 2008, Péran et al., 2003, 2009). Broca’s aphasic patients also tend to rely on nouns, resulting in a reduced verb production (Bastiaanse & Jonkers, 1998; Kim & Thompson, 2000; Thompson, Lange, Schneider, & Shapiro, 1997).

Secondly, both PD patients (Illes et al., 1988) and agrammatic aphasic individuals (Saffran et al., 1989; Thompson & Shapiro, 1995) have great difficulty producing complex sentences in which NPs are not in their base position.

Third, semantic information consistently facilitates sentence comprehension in PD (Grossman et al., 1991, 1992a; Hochstadt et al., 2006; Lieberman, 1989; Lieberman et al., 1992; Natsopoulos et al., 1993) and in Broca’s aphasia (Blumstein, 1995). This suggests that in both patient groups, procedural knowledge of grammar is affected, whereas declarative memory is preserved (Friederici, Kotz, Werheid, Hein, & Von Cramon, 2003).

Fourth, Lieberman et al. (1992) analyzed the speech production in PD patients and concluded that the phonetic characteristics of the speech output of PD patients were similar to those of Broca’s aphasic patients (Hochstadt et al., 2006; Lieberman, 2000, 2006). In addition, Hochstadt et al. (2006) concluded that motor speech disorders in PD seem to have an influence on higher cognitive functions such as the rehearsal process of verbal WM which, in turn, affects sentence comprehension.
Fifth, reduced capacity to simultaneously speak and monitor one’s own speech could account for the self-monitoring impairments found in both Broca’s aphasia and PD (Oomen, Postma, & Kolk, 2005, see Figure 3.1).

Sixth, PD patients with comprehension problems have slowed lexical retrieval (e.g., Grossman, et al., 2002b) comparable to what was already reported in Broca’s aphasic patients (Swinney et al., 1996; Zurif et al., 1993).

Finally, in both patient groups, a causal link between sequential learning and language performance has been described (Dominey et al., 2003; Lieberman, 2006, 2007; Sirigu et al., 1998). We focus here on the syntactic sequencing deficits of Broca’s aphasic patients, since sequencing in PD will be discussed in more detail in the next section. Dominey, Hoen, Blanc, & Lelekov-Boissard (2003) for example, found that while the processing of serial order remained largely intact in Broca’s aphasic patients, the processing of systematic rule-based transformations as required for both non-canonical sentences and abstract sequences were impaired.

Moreover, besides their deficits in production and comprehension, Broca’s aphasic patients often show impairments in the expression of motor skills (i.e., ideomotor apraxia13) (Wang & Goodglass, 1992), just like PD patients do.

To conclude, the question of whether the underlying causes of the language problems in Broca's aphasia and PD are similar is still unanswered and can be rephrased as whether the language deficits in PD are caused by an underlying linguistic deficit, as seen in Broca's aphasia, or by their executive or sequencing dysfunctions that are known to be part of PD.

### 3.5 Theories on the involvement of the basal ganglia in morphosyntactic processing

In the following section, we will focus on theories hypothesizing on the involvement of the BG in morphosyntactic processing.

**Basal ganglia as a sequencing engine**

Lieberman (2000, 2006, 2007) investigated PD patients’ language processing as a means to theorize about the role played by the BG in language processing, but mainly discussed his theory on the neural basis of language in an evolutionary framework, remaining loyal to the ‘struggle for existence’ mechanisms of evolution noted by Charles Darwin (1859). Lieberman (2000, 2006) presented evidence that the reiterative ability14 characteristic for human language is linked and probably derived from elements of neural circuits that regulate motor control. In other words, the neural circuitry involved in motor control has been modified

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13 The term ‘apraxia’ encompasses various disorders affecting the purposeful execution of deliberate movements which cannot be explained by elementary motor-sensory deficits, perceptual and comprehension impairment or severe mental deterioration. ‘Ideomotor apraxia’ is a form of apraxia in which the implementation of the gesture in a precise motor programme is disrupted (De Renzi, 1989).

14 The reiterative ability is the ability to combine a finite number of words to generate an infinite number of sentences. This ability is often called recursion (Hauser, Chomsky, & Fitch, 2002).
through evolution to be involved in the sequential process of language and other human cognitive functions.

Furthermore, Lieberman claims that since the neural basis of language is intertwined with other aspects of cognition, motor control and emotion, it cannot be modular in nature as claimed by modular theorists such as Fodor (1983) and Pinker (1998, 2002). In contrast to Lieberman’s model, modular linguistic and psycholinguistic theories defend the idea that language modules in the brain are encapsulated and hypothetically regulate only one specific aspect of language, analogous to computer systems. Lieberman’s hypothesis on the role of the BG in language processing is based on the assumption that the brain works at two levels to perform human behavior such as talking or comprehending a sentence. At the first level, isolated regions of the brain perform ‘local operations’. However, the neural region that performs a local operation does not in itself constitute the behavior. Instead, at a second level, many local operations in anatomically separated neural structures which are linked in circuits are needed to yield observable behavior. Lieberman (2006) focused on the activating or inhibiting ‘local operations’ performed by the BG within the cortico-striato-cortical circuits. Lieberman (2006, 2007) defined the BG as a ‘sequencing engine’ that can reiterate ‘motor pattern generators’ as well as ‘cognitive pattern generators’. Applied to syntax, the BG can thus generate an infinite number of possible sentences by combining a finite set of words using a finite set of rules (Lieberman, 2006, 2007). According to Lieberman, in PD patients, these local operations performed by the BG in the cortico-striato-cortical circuits are disturbed and cause their comprehension deficits.

*Declarative-Procedural hypothesis*

Ullman et al., (1997) found a correlation between the right-sided hypokinesis of PD patients and their difficulties in the production of the regular English past tense. As regular forms are thought to be generated by grammatical rules, the authors concluded the BG and frontal cortex together constitute the ‘procedural memory’ system that regulates morphosyntactic aspects of language. Irregular verbs, however, are retrieved from the lexicon, which is part of a temporal-parietal/temporal/parietal ‘declarative memory’ system. According to Ullman and colleagues (Ullman, 2001; Ullman et al., 1997) the deficit arising from BG damage is automatic in nature, as it affects the automatic procedural rule system of grammar. The existence of this dual-route mechanism, in which the frontal BG rule system is involved in the computation of suffixed regular inflected forms and a medial temporal/parietal circuit responsible for processing irregular inflected forms, was confirmed by data from neuroimaging experiments. These imaging studies reported that the left frontal area, in particular the left inferior frontal gyrus (IFG), plays a crucial role in processing inflected words (Miceli, Silveri, Romani, & Caramazza, 1989; Miceli et al., 2002; Novoa & Ardila, 1987; Shapiro & Caramazza, 2003; Tyler et al., 2002).

*The domain-general inhibitory role of the basal ganglia*

In their replication study of the original Ullman et al. (1997) experiment, Longworth, Keenan, Barker, Marslen-Wilson, and Tyler (2005) found a tendency in English speaking PD patients to perseverate on the cue (i.e., verb stem) rather than to produce a past tense as requested. In addition, Longworth et al. (2005) have argued that patients with lesions in the BG may have separate deficits in semantic and syntactic processes. Similarly, the language problems in PD discussed in the previous section of this chapter revealed both semantic retrieval and
syntactic processing deficits, which supports a role for the BG in both processes and not only in the rule governed syntactic processes.

The findings of Longworth et al. (2005) suggested that the BG play a restricted, non-language-specific, inhibitory role (i.e., inhibition of competing alternatives) in the later controlled stages involved in language comprehension and production. Particularly for lexical activation and by carrying out a semantic priming task, Copland (2003) concluded that at the long inter-stimulus interval, PD patients, did not show suppression of the infrequent meaning of homophones (or in other words could not facilitate the dominant meaning). Copland related this result to an impairment of inhibitory mechanisms in PD. Crescentini et al. (2008, 2010) proposed a similar inhibitory role of the BG in word generation. Using functional Magnetic Resonance Imaging (fMRI), Crescentini, Shallice and Macaluso (2010) aimed at elucidating the role of selection and association within the cortico-striato-cortical circuits during verb and noun production in healthy controls. The BG were found to be particularly active during verb production in the high selection condition (i.e., items without any clearly dominant response), irrespective of the association strength. This activation of the BG is in agreement with a role of the BG in inhibiting competing alternatives (e.g., Longworth et al., 2005) during response selection, but according to the authors can also be related to their contribution in emphasizing task-relevant information (McNab & Klingberg, 2008).

**Role of the basal ganglia in the late integrational phases of syntactic processing**

In contrast to the conclusions of Ullman et al. (1997), the electrophysiological evidence of Kotz and colleagues (Friederici, Von Cramon, & Kotz, 1999; Friederici, Kotz, Werheid, Hein, & Von Cramon, 2003; Frisch, Kotz, Von Cramon, & Friederici, 2003; Kotz, Frisch, Von Cramon, Friederici, 2003) suggested a functional dissociation of the left cortical and subcortical parts of the frontal BG system, instead of treating the subcortical parts in tandem with the cortical parts to represent the procedural grammatical system.

In a series of several Event Related Potential (ERP) studies, Kotz and collaborators (Friederici et al., 1999, 2003; Frisch et al., 2003; Kotz et al., 2003) used different syntactic structures to investigate grammatical processing in two BG patient populations, that is, patients with a focal BG lesion and PD patients. As will be discussed in more detail in Chapter 6 (section 6.2.2, p. 85), the results of these electrophysiological experiments confirmed the differential involvement of the left frontolateral cortex and not the BG in early automatic aspects of grammatical processing. According to Friederici et al. (2003), the alteration in the P600 reflected distortions of the late controlled syntactic integration processes in PD. The left frontal cortex and the left anterior temporal cortex contribute jointly to the early automatic processing underlying the (E)LAN, whereas the left BG contribute to the late controlled syntactic integration processes underlying the P600 as evidenced by the reduction of the P600 effect in patients with focal BG lesions or PD. (Friederici & Kotz, 2003; Friederici et al., 2003).
3.6 The research questions of this thesis

The basic theme of this thesis concerns the question of ‘how’ the BG system is involved in syntactic processing during comprehension and production.

As reviewed in this chapter, there is abundant evidence that the BG are involved in language processing. It is clear that PD patients demonstrate difficulty in language processing. Furthermore, specific syntactic language deficits, both for production and comprehension, accompany BG lesions (Brunner, Kornhuber, Seemuller, Suger, & Wallesch, 1982; Damasio & Damasio, 1992; Fabbro, Clarici, & Bava, 1996; Hochstenbach, Spaendonck, Cools, Horstink, & Mulder, 1998; Pickett, Kuniholm, Protopapas, Friedman, & Lieberman, 1998). Additional clinical underpinning for the proposed involvement of the BG in language processing comes from several other empirical sources including: 1) the effects after deep brain stimulation and surgically induced lesions of the BG; 2) the findings of ERP studies in PD; and 3) neuroimaging reports on the involvement of the BG in language processing in NBDS.

In the next section, the research questions of this thesis concerning the involvement of the BG system in language are put forward.

3.6.1 Language and sequential processing: implications for PD

It is a fact that language is bound to a linear pattern. As an example, we cannot speak two or more words at a time; words have to come out in a linear sequence. The rules of grammar specify the possible sequential order of words in a sentence. Hierarchical syntactic structures are built as sequences of combinations of word categories constrained by the intrinsic structure of language. There is an obvious link between sequential learning and language: both involve the extraction and further handling of elements occurring in temporal sequences. Thus, language is a higher cognitive function in which sequencing is inherently present at multiple structural dimensions: in phonology, morphology, syntax and discourse.

Putting actions in the proper order is also fundamental to motor control. It can thus be concluded that sequential processing is highly relevant to both motor and language processing. This conclusion is, however, not new. Already in 1951, Karl Lashley suggested that neural mechanisms that were initially adapted for motor control are the basis for syntax and other aspects of human cognition. Lashley was following in the footsteps of Charles Darwin, who noted that “an organ might be modified for some other and quite distinct purpose” (Darwin 1859, p. 190). Recently, strong evidence has been given that sequential learning played a crucial role in the evolution of language (Conway & Christiansen, 2001; Greenfield, 1991; Lieberman, 2002).

Lieberman (2006) suggested that “the ability to reiterate or reprogram a finite set of automatic acts appears to be one of the keys to both articulate human speech and syntax, as well as to the flexibility and creativeness of human thought processes” (p. 11). The cortico-striato-cortical circuits yield this reiterative or recursion ability (Lieberman, 2006). Lieberman (2006, 2007) described the BG complex as ‘a sequencing engine’. In his view, the direct and indirect pathways through the BG system activate or inhibit motor or cognitive pattern
generators. Applied to syntax, the BG can thus generate an infinite number of possible sentences by combining a finite set of words using a finite set of rules (Lieberman, 2006, 2007). Within syntactic processing, the BG then switch from one linguistic subprocess to the next at the right moment in time. Likewise, Steedman (2002) elaborated on the common sequencing aspect of motor actions and syntax and argued that the syntactic aspect of the language faculty derives from a set of operations originally developed for motor planning.

According to the theory of Mink (1996) for motor control, the BG provide a gating mechanism in action selection, such that only the selected motor program is initiated, executed and terminated at the appropriate timing, whereas other competing programs are inhibited. As part of the cortico‐striato‐cortical circuits, the BG help to encode goal‐oriented action sequences through behavioral learning and are engaged in the retrieval, management, and constitution of these sequences (Graybiel, 1995a, 1995b, 1997). Hence, Graybiel (1997) defined the BG as ‘cognitive pattern generators’. The BG do not initiate or generate syntactic sequences (Aldridge, Berridge, & Rosen, 2004) but enable the coordination and orchestration of these sequences by momentarily inhibiting or disinhibiting particular frontal cortical areas.

In line with the involvement of the BG in action selection (Mink, 1996), it has been hypothesized that during sentence processing, the BG contribute to a selective gating (or filtering) of relevant information into WM by inhibiting or disinhibiting the prefrontal cortex (Frank, Loughry, & O’Reilly, 2001; McNab & Klingberg, 2008). According to this hypothesis, PD patients, who have dysfunctional BG, have disturbed filtering of lexical‐syntactic information into WM, which might in turn complicate their sentence comprehension for complex sentences.

The frontal cortex is known to be subdivided for sequence processes on distinctive forms of knowledge representation. Different kinds of linguistic information are sequentially processed in Broca’s area during speech production (Sahin, Pinker, Cash, Schomer, & Halgren, 2009; Sirigu et al., 1998), while motor action planning is processed in the prefrontal cortex (Sirigu et al. 1998). PD is a progressive, degenerative neurological disease that indirectly affects the frontal cortex through the patient’s dysfunctional cortico‐striato‐cortical circuits. Knowing that Broca’s area is involved in both language production and comprehension it is not unexpected that PD patients show simultaneous disorders in planning and language processing since the BG are supposed to be functionally connected to different regions in the frontal cortex. Important to mention is that Broca’s area is embedded in different cortical networks that contribute to other cognitive domains than language, such as action perception and execution (Koski et al., 2002) and imitation (Iacoboni et al., 1999). It thus seems that Broca’s area has a role in the processing of goal‐directed actions that goes beyond the language domain.
This leads to the first major question addressed in this thesis:

| Is syntactic sequencing during comprehension and production of sentences disturbed in patients with mild to moderate PD who are known to have difficulties in performing sequences of voluntary movements? |

A detailed characterization of PD patients’ linguistic deficits can contribute to hypotheses on the involvement of the BG in sentence comprehension and production. Thus, to gain further insight in the involvement of the BG in syntactic sequential processing, we investigated in a group of PD patients the influence of dysfunctional cortico-striato-cortical circuits on verb inflection in sentence context (Chapter 4) and on the comprehension of sentences in which the factors of canonicity and length were manipulated (Chapter 5). Furthermore, to explore the neural mechanisms of sequential processing further an fMRI-experiment was conducted. fMRI provides a means of interpreting how the BG contributed to the mediation of sequential processing of word order and grammaticality in NBDS with intact cortico-striato-cortical circuits (see Chapter 7) and in patients with PD (see Chapter 8).

We expect an impairment for comprehension of non-canonical sentences in PD because of the involvement of BG in the detection of sequential order of the sentence components (Lieberman, 2006, 2007), which is related to sequencing in action cognition (Graybiel, 1995a, 1995b, 1997).

3.6.2 Language and executive functions: implications for PD

The coexistence of motor problems, executive dysfunctions and language processing deficits in non-demented PD patients suggests that the neural bases of language and cognition are commingled with aspects of motor control through their evolutionary history (Lieberman, 2006, 2007).

Thus, a second major issue we have to address concerns the interaction between motor, cognitive and language functions. Researchers in the tradition of modular theories of mind define syntax as an ‘encapsulated’ brain system that operates automatically and independently of other cognitive processes (Fodor, 1983; Pinker, 1994). However, computational neuroscientists assume an interaction between linguistic and other cognitive processes, implying interactions at all levels of information processing, including syntax (e.g., Elman et al., 1996).

The reduction of PD patients’ spontaneous production to simple sentences may reflect concomitant cognitive and motor speech impairments, rather than being a pure language deficit (Murray & Lenz, 2001). Hochstadt et al. (2006), among others, described a syntactic comprehension deficit for syntactically complex sentences. Interestingly, they also found a correlation between this comprehension deficit and the impairment in cognitive set-switching, in motor function (Hoehn & Yahr stage), and in reading span (i.e., verbal WM).
Thus, the second major question of this thesis can be formulated as follows:

Does language sequencing interact with other cognitive processes, i.e., executive functioning in PD patients with obvious motor disorders?

PD disrupts both controlled and automatic behavior. Contrary to other researchers (Arnott et al., 2001; Friederici & Kotz, 2003; Friederici et al., 2003; Longworth et al., 2005) we expected PD patients to exhibit disorders in both the automatic and the controlled aspects of language processing during sentence comprehension and production. Accordingly, we proposed that the BG are engaged in the automatic execution of syntactic sequences, but are also engaged in the controlled reordering or altering of cortically driven syntactic processes.

We were able to reveal the possible influence of executive functions on PD patients’ verb production (Chapter 4) and sentence comprehension (Chapter 5).

The off-line behavioral experiment described in Chapter 4 studied verb retrieval and sentence integration processes simultaneously by manipulating the grammatical features of the test sentences. We aimed to verify whether impairments were due to a linguistic deficit per se, or whether they were the consequence of another cognitive deficit. The study compared a group of Dutch-speaking PD patients with a group of HC subjects matched for age, gender and education. The verb production performances of the PD patients were correlated to their scores on executive function tasks. In addition, the correlation between PD patients’ clinical features with verb production in sentence context gave us more information on the effects of BG dysfunction and dopaminergic therapy.

Chapter 5 describes the behavioral experiments that were used to test the interaction between executive functioning and sentence comprehension in Dutch speaking PD patients compared to age- and education-matched HC subjects. The sentence materials of the picture verification task focused on the difference between active and passive sentences. Moreover, instead of testing the interaction of one particular part of executive functioning with sentence comprehension, this study assessed a complete range of executive functions relevant to sentence comprehension, including attention, WM, set switching, inhibition and abstract sequencing abilities. Since executive function is hypothesized to underlie effective sentence processing, relationships between these separate executive functions and sentence comprehension were expected for both groups. However, due to the dysfunctional cortico-striato-cortical circuits in PD these relations are expected to be more visible in the diseased population and thus to strongly reflect the effects of executive dysfunction.

The goal of the event-related fMRI study described in Chapters 7 and 8 was to further investigate the involvement of BG and IFG in the automatic processing of correct sentences compared to the more controlled processing of syntactically violated sentences. In Chapter 8, PD patients were compared to age- and education-matched HC subjects that were also similar in their cognitive switching and WM abilities.