In this thesis the question of how the basal ganglia (BG) system is involved in syntactic processing during comprehension and production in patients with Parkinson’s disease (PD) was investigated. In the following section the introductory chapters to this thesis and the results obtained from our experiments, described in Chapters 4, 5, 7 and 8, will be summarized. For a general conclusion on the results of our studies we refer to Chapter 9.

Chapter 1 consists of a general introduction to PD and also includes a review of the Dutch linguistic background of the studies described in this thesis. Of importance to our research were word order, verbs and their inflections and the influence of these linguistic variables on sentence comprehension and production of Dutch-speaking PD patients.

Chapter 2 is dedicated to reviewing the neuropathology and cognitive symptoms of PD patients. In general, PD is described as a progressive, degenerative neurological disease in which the dopaminergic afferents to the striatum are lost and striatal output via the direct and indirect pathways is altered (see Figure 2.5, p. 16). As a result, PD patients demonstrate non-motor symptoms (Dubois & Pillon, 1995, 1997) in addition to their cardinal motor symptoms (Wolters & Bosboom, 2007).

The direct and indirect pathways model suggests that both pathways control the initiation, switching, modulation and termination of actions that are aspects of serial processing (Saint-Cyr, 2003). It is widely accepted that the BG are involved in the selection of appropriate actions in response to both external and internal stimuli. 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). Hence, Graybiel (1997) defined the BG as ‘cognitive pattern generators’. The BG do have a role in the implementation of the process, but the initiation and programming of the sequence occurs elsewhere in the brain (Aldridge & Bertridge, 2003). However, next to sequencing, “processing of context” is also described as being a cognitive function of the BG (Saint-Cyr, 2003). The reduction of dopamine in the striatum in PD prevents the striatal nuclei from encoding cortically coded contexts. Consequently, the BG are not able to select successful (rewarding) activation patterns in the output structures, which facilitate processing routines in the frontal cortex.

Neuropsychological deficits frequently occur in PD, even in early, untreated PD patients (Aarsland, Bronnick, Larsen, Tysnes, & Alves, 2009). Domains that are typically affected include executive functions, attention, memory, and visuospatial skills (Dubois & Pillon, 1995, 1997; Green et al., 2002; Muslimovic, Post, Speelman, & Schmand, 2005; Pillon, Czernicki, & Dubois, 2003). Moreover, Koerts (2009) and Koerts, Leenders, and Brouwer
(2009) suggested that patients with PD have both impaired controlled (i.e., central executive) and automatic information processing. PD has been described as a de-automatization disorder, since reliance on automatic processing decreases while they compensate this with an increased reliance on cognitive control (Saling & Phillips, 2007). Although the focus of many cognitive studies is on the typically disturbed executive functions deficits, we also expect to find alterations in automatic linguistic routines. In Chapter 2, the comprehensive mental schema framework of Koerts et al. (2009) was used to illustrate the dynamic relations between 1) subprocesses of the ‘Supervisory Attentional System’ (SAS), which is closely tied to the prefrontal cortex and 2) automatic processing, which relies more on the BG system (see Figure 2.6, p. 19).

Furthermore, as described in Chapter 3, disturbed cortico-striato-cortical circuits also influence different aspects of language processing. Before extensively reviewing PD patients’ language deficits, Levelt's speech production model was introduced (1983, 1989, see Figure 3.1 p. 26). Levelt’s model clarifies both production and comprehension of spoken language and implements the distinction between controlled and automatic processing, which is similarly implemented in the mental schema framework of Koerts et al. (2009, see Figure 2.6, p. 19). Levelt’s Conceptualizer as well as Monitoring involve highly controlled processing, whereas all the other components in the processing model are largely automatic. Thus, the Monitor, as a central subprocess of the SAS (see Figure 2.6, p. 19), screens ongoing behavior based on information on context and content aspects of a stimulus, which sometimes activates the system above the horizontal bar. Related to the Monitor of the SAS is the Monitoring during speech production as implemented in the model of Levelt. In short, both internal speech (‘internal loop’) and overt speech (‘external loop’) are fed into the Speech Comprehension System for checking purposes during production of speech (see Figure 3.1, p. 26). Analogously, Van Herten (2006), Van Herten, Chwilla and Kolk (2006), Kuperberg (2007) and Vissers (2008) proposed a similar monitoring process during comprehension. Embedding existing reports on language deficits in PD within Levelt’s model and its extensions, it was concluded that PD patients display: 1) disturbed speech monitoring (McNamara, Obler Au, Durso, & Albert , 1992), 2) reduced sensitivity to linguistic context causing comprehension deficits (e.g., Whiting, Copland, & Angwin , 2005) and 3) lexical retrieval deficits (e.g., Auriacombe et al., 1993).

Chapter 3 is also dedicated to understanding the contribution of the distinct parts of the cortico-striato-cortical circuits (i.e., frontal areas and BG) to language processing. Therefore, we report on the results of studies clarifying the similarities and differences between the language deficits in PD and Broca’s aphasia. Based on this review, the question of whether the underlying causes of the language problems in Broca’s aphasia and PD are similar 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.

Before formulating our own research questions, an overview is given of the existing theories on the involvement of the BG in morphosyntactic processing. Among these theories is the suggestion of Friederici, Kotz, Werheid, Hein, and Von Cramon (2003) that the BG support late and controlled syntactic integrational processes, rather than early automatic structure building processes, as evidenced by the reduction of the P600 effect in patients with focal BG lesions or PD. Hochstadt (2009) interpreted the reduced P600 effect in PD as reflecting
“difficulty with not just syntactic integration but integration with context more broadly”. Thus, PD patients might not experience the conflict between heuristics and syntactic processing to begin with. Research showed that PD compromises both the automatic (Angwin et al., 2004; 2005; 2007) and the controlled aspects (Arnott, Chenery, Murdoch, & Silburn, 2001; Copland, 2003; Copland, Chenery, & Murdoch, 2000) of for example semantic processing. Combining the reviewed literature on the cognitive symptoms (see Chapter 2, section 2.8) and language deficits (see Chapter 3, section 3.3) and in contradiction to Friederici et al. (2003) we hypothesize that PD not only disturbs the more controlled, planned processing aspects of comprehension and production, but logically also the automatic aspects. In general, we suggest that because of failing automaticity, PD patients rely more on the cortically represented executive functions when processing language. Based on the discussed evidence of language impairment in PD, one could hypothesize that the BG engage in the automatic execution of syntactic sequences, but are also engaged in the controlled reordering or altering of cortically driven syntactic processes.

Finally, Chapter 3 is concluded with the formulation of two research questions:

1) 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?

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

The experiments discussed in the chapters of this thesis aimed at answering these research questions.

The main goal of the study described in Chapter 4 was, to explore the relation between possible verb-in-sentence-context deficits and executive functions that are relevant for sentence processing. To investigate this, the performance of a group of Dutch speaking PD patients was compared with a group of healthy control (HC) participants on an un-timed verb in sentence context task. The test sentences were developed by manipulating three linguistic variables: 1) finiteness, 2) position of the verb and 3) tense. In addition, several executive functions were assessed and related to the score on the verb production ability-scale. For the statistical analyses the Mokken model (Mokken, 1971) was used to analyze the performance of all subjects on the verb production task. In this way, a verb production ability-scale was estimated with persons and items on the scale, indicating the ability of each person, and the difficulty of each item. This makes it possible to compare persons, but also items with each other. Furthermore, non-parametric (Spearman) correlations between the score on the ability-scale and the scores on the cognitive tests as well as their relevant clinical features were computed. The results showed that PD patients performed worse than the HCs on the verb production ability-scale. It is suggested that due to a failing automaticity of verb production, PD patients need to rely more on the cortical represented executive functions, which, unfortunately, are also dysfunctional. The findings of this study evidenced that a working memory (WM) overload and set switching impairments can lead to verb production deficits in PD. Our data put forward WM and set switching impairments as key factors of the verb production deficits in PD.
Coexistent impairment in executive functions and language comprehension in PD patients has been repeatedly observed. In Chapter 5, the hypothesis that executive dysfunctions are involved in sentence comprehension deficits in PD is further explored. To this end, sentence comprehension using a self developed ‘picture-verification task’ and also executive functions were assessed in Dutch-speaking PD patients and HC subjects. Two aspects of the sentence materials were varied: 1) phrase structure complexity and 2) sentence length in trials that had participants judge whether or not a spoken sentence matched a picture. The design used in this experiment is a 2 (syntactic complexity) x 2 (length) x 2 (matching) within-subjects’ repeated measures design. Since Friedman’s test for ranks does not allow for the examination of interaction effects, a non-parametric statistical method to examine the main and interaction effects was proposed. The total sentence comprehension score of PD patients and HC participants was compared using the Mann-Whitney U test. Main effects and interaction effects between the different manipulations within the sentence comprehension task (phrase structure complexity, sentence length and whether or not a spoken sentence matched a picture) were investigated. In addition, hypothesis-driven Spearman correlations between the total scores and subscores on the sentence comprehension task and the scores on the cognitive tests of the PD patients were computed. Overall, it could be concluded that PD patients do not have a specific comprehension deficit limited to one aspect of the sentences, i.e., dealing with long or non-canonical structures, suggesting that the language impairment in PD patients is not of a specific aspect of language processing. Instead, the patients showed a more non-specific comprehension impairment, and the pattern of errors was identical with that found in the HC group. These deficits appear to be dependent on executive functions. Deficits in sustained visual attention appear to underlie their overall comprehension deficit, possibly due to the demands of the picture-sentence matching task. Last, decreased set-switching, inhibition, and WM abilities all were associated with difficulties in comprehending non-canonical passive sentences, rather than one specific aspect of executive function being primarily associated with the difficulties of these sentences. Generally, our study confirms that there does not appear to be a language faculty independent from executive control.

In Chapter 6, as an introduction to the imaging studies described in Chapters 7 and 8, a brief introduction to the Event Related Potential (ERP) and functional Magnetic Resonance Imaging (fMRI) technique is given. Subsequently, the studies evaluating sentence comprehension in PD are reported separately for ERP and fMRI. Prior to presenting these linguistic imaging studies in PD, which are relatively scarce, an overview is provided on ERP measurements in BG-lesioned patients and relevant fMRI studies showing activation in the BG and frontal cortex during violation processing.

In Chapter 7 a mixed block/event related fMRI study was presented, which examined the respective roles of the inferior frontal and subcortical parts (i.e., BG) of cortico-striato-cortical circuits in comprehension of written sentence materials in which the variables of word order and grammaticality were factorially manipulated. The experiment was conducted in fifteen right-handed healthy elderly individuals. The participants were instructed to read Dutch sentences in the active or passive voice that were either correct or contained a grammatical violation (i.e., inflectional violation or verb-argument structure violation). The region of interest (ROI) analysis of prespecified subparts of the inferior frontal gyrus (IFG) and BG showed a main effect of word order in the right pallidum, in which more activation was elicited by active sentences than passive sentences. The pars opercularis (BA
44) and the pars triangularis (BA 45) of the IFG showed similar interaction effects between grammaticality and canonicity. For the right BA 45 and to a lesser extent the pars orbitalis of the IFG (BA 47), however, a clear main effect of grammaticality was found. Possibly, these areas are involved in a semantic processing strategy used by the participants. The results suggested distinct roles for the IFG and BG in the comprehension of sentences in which canonicity and grammaticality were varied. Our findings furthermore demonstrated that right hemispheric activation is prominent in healthy elderly participants.

Whereas the experiment described in Chapter 7 focused on the comprehension of written sentence materials of HC subjects, the experiment in Chapter 8 addressed the consequences of PD patients’ striatal dopamine depletion on the patterns of activation during the comprehension of these sentences. In contradiction to our expectations, PD patients showed a word order effect in their right putamen compared to HC subjects. However, a main effect of canonicity was found in the right pallidum for the HC subjects only, suggesting that PD patients fail to exploit sequential syntactic information and possibly lose their capacity to use heuristic routines in the comprehension of the canonical active sentences. Moreover, PD patients did not engage their left middle temporal gyrus (MTG, BA 21) to process passive sentences, since a canonicity effect was only evident in the BA 21 for the HC subjects. However, they recruited additional prefrontal cortex (PFC) when processing passive sentences: the BA 10 for passives compared to actives. Activation in the PFC BA 10 during the processing of passive sentences was explained in three different ways. First as a compensatory mechanism, implying that PD patients relied on the executive control component of WM. Secondly, PD patients might have relied on a plausibility strategy, based on Theory-of-Mind (ToM) reasoning. And finally, activation in PFC BA 10 might have reflected a semantic strategy for dealing with word order information in passive sentences.

In addition, PD patients showed a main effect of grammaticality in the pallidum and the left putamen. Also, a clear grammaticality effect, independent of canonicity, was found in the bilateral BA 44 and BA 45. These grammaticality effects were based on the higher activation for the sentences containing an inflectional violation compared to the other types of violation. One possibility is that the patients noticed the inflectional violation solely on the basis of the physical visual features of the shorter verb segment during the highly automatic first-pass parsing processes. In the BA 47, a clear opposite pattern of activation was evident for the two groups. PD patients apparently relied more on this inferior frontal area for the violated sentences than for the non-violated sentences. HC subjects activated the BA 47 more for the non-violated sentences as compared to the violated sentences. Compared to the HC subjects, PD patients apparently have difficulties with the monitoring processes in reaction to the violation in the sentence. Instead, PD patients try to integrate the violated participle in the sentence relying on their semantic executive system, which produces some difficulty and greater activation of this area. Our results are in line with the suggestion of Hochstadt (2009) that PD patients have deficits in the late phase of sentence processing, in which monitoring of the violation is lacking. In other words, PD patients have an impairment of their central monitor and might not experience the violations in the first place.