Chapter 4

Cognitive dysfunction in Parkinson's disease: controlled and automatic behavior

Janneke Koerts, Klaus L. Leenders & Wiebo H. Brouwer

Cortex: in revision

4.1 Abstract

In this review the evidence is described with regard to impaired automatic and controlled information processing in cognitive functioning of patients with Parkinson's Disease (PD), using a comprehensive mental schema framework. PD patients show impairments applying and achieving automaticity. Studies suggest that the latter could be due to an inability to shift from cortical to subcortical areas when controlled processing becomes automatic. Specifically, PD patients show impairments when learning was based upon feedback, which in turn is influenced by the use of levodopa.

In addition, PD patients show impairments in cognitive control or executive functions, specifically in cognitive flexibility, planning, working memory, effort, motivation and inhibition. Neuroimaging studies show decreased activation of the fronto-striatal circuits and increased prefrontal activation, suggesting a compensatory mechanism reflected by cortico-cortical and subcortical-cortical shifts. Moreover, treatment strategies, such as the use of levodopa and subthalamic nucleus deep brain stimulation, influence executive functions in PD.

Thus, the cognitive impairments observed in PD, both at the level of automatic and controlled processing, are the result of a complex interplay between dopaminergic dysfunction of the fronto-striatal circuits, compensatory mechanisms and treatment strategies applied in PD.

4.2 Introduction

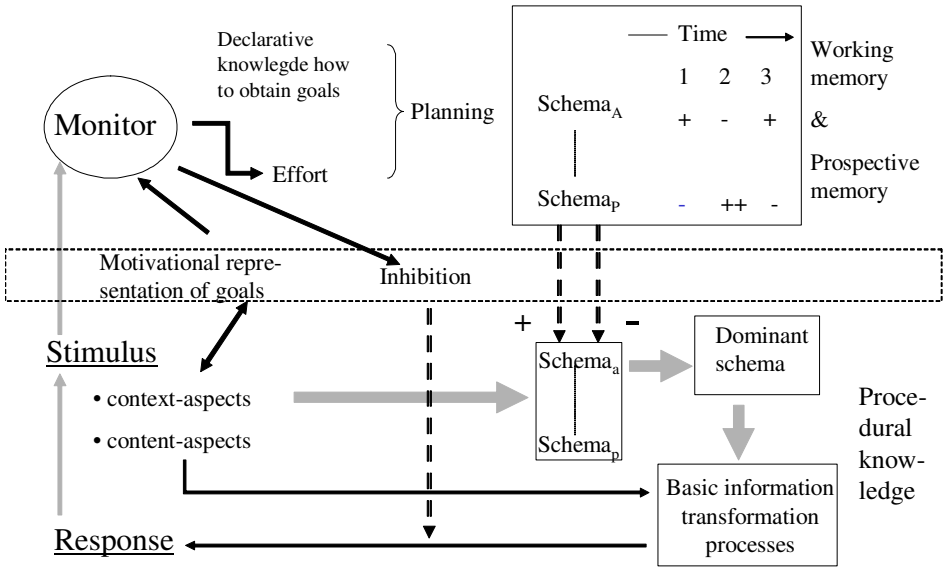
Parkinson's disease (PD) is characterized by a dopaminergic depletion in the fronto-striatal circuits (see figure 1.1), leading to impaired motor and cognitive functioning. In the domain of motor functioning, impairments appear to be strongest in seemingly automatic routine aspects of movement like global postural adjustments, while consciously-controlled goal-directed single joint movements are relatively preserved. However, in the domain of cognitive functioning, impairments of automatic processing are less often reported and the focus of many studies is on impairments of executive functions which are typically described as voluntary, consciously controlled, and goal-directed. The purpose of this review is to describe the evidence with regard to impaired automatic and controlled information processing in cognition in PD, using a comprehensive mental schema framework.

Behavior can be defined as all actions in response to external or internal stimuli. These actions can be regulated automatically, e.g. in an *experienced* driver, or in a (consciously) controlled manner, e.g. in an *inexperienced* driver. Action regulation is not an all or nothing matter, it is assumed that in all activities there is a mix of automatic and controlled regulation. In routine situations automatic processes take advantage of previously established and learned relationships between external or internal contexts and behavioral patterns. The implicit memory representations of these context specific behavioral patterns are called schemata (Norman & Shallice, 1986). Norman and Shallice assume that all behavior is caused by the interaction of external and internal stimuli and schemata.

Controlled processing concerns deliberate planning and regulation in situations where current schemata are not sufficient. It requires maintenance and stabilization of goal representations in working or prospective memory and the flexibility to update these goal representation when necessary (Cools, 2008). Also the inhibition of automated responses and retrieval from declarative memory are involved. The complex cognitive function that Norman and Shallice describe to regulate controlled processing is the Supervisory Attentional System (SAS). The SAS function is closely tied to the prefrontal cortex. Ultimately the SAS has its effect on behavior by selectively inhibiting and facilitating already existing schemata. In the process new schemata are formed and learned, also dependent on the effects of their application (reinforcement). To be able to control behavior the SAS is assumed to have a number of constituent more elementary functions (Norman & Shallice, 1986), like monitoring, planning, cognitive flexibility and divided attention. Declarative memory and working memory also play an important role and assist respectively in the planning, implementation and application of new schemata.

The dynamic relations between the different subprocesses of the SAS, and automatic processing are depicted in figure 4.1, adapted from Brouwer and Schmidt (2002). We will use this comprehensive framework[2] to assess the evidence with regard to impairments in automatic and controlled processing in PD. In addition, this framework can be used to determine which cognitive impairments are primary and which are secondary in PD. It was developed in an attempt to better accommodate the relationships between motivational and emotional factors and executive functions, which are so evident in patients with orbitofrontal damage, and Brouwer & Schmidt (2002) thus explicitly included motivation and emotion into the SAS framework. A simple example with regard to the effect of motivation on monitoring concerns someone who recently stopped smoking. This person is much more sensitive to triggers like left about butts and cigarette boxes than when he was still smoking. Similar logic can be applied to other forms of motivation.

Figure 4.1 Schematic representation of subprocesses of automatic and controlled behavior (adapted from Brouwer & Schmidt (2002)



[2] A framework is composed of general claims about cognition and is insufficiently specified to enable predictions to be derived from them. In this respect a framework differs from a model, which can be defined as framework with assumptions about its application to a specific situation (Anderson, 1993). A model is thus specific for a certain situation, whereas a framework is a more general construction.

The system below the horizontal bar represents the routine selection of behavior, e.g. automatic processes. In these situations a dominant schema will be activated. A distinction is made between context and content aspects of sensory input. Context aspects are those elements of a stimulus or situation that trigger schemata learned to be appropriate for that situation and its predicted progression. Content aspects on the other hand are elements that can vary within the situation. For example, when driving towards an intersection (context), the schema for handling an intersection is elicited. The other traffic and characteristics of the road (content) subsequently define within this schema where to look and how to act. In any situation, triggers for many different schemata are available. Which schemata become active in regulating behavior is determined by contention scheduling (the schema with the strongest activation wins) and lateral facilitation and inhibition between schemata (Shallice, 1988).

The system above the horizontal bar represents the SAS, which is used in non-routine situations. Assumedly, the situation, including the effects of own behavior, is continuously screened with regard to motivational or emotional risk by the monitor function. If a challenge to important biological goals (for example a threat to social status or an opportunity to improve it) is sensed, ongoing behavior is inhibited and the SAS is switched on further. Motivated by the need to neutralize the threat or to realize the opportunity (effort), a plan is retrieved from declarative memory, adapted (planning) and scheduled in working memory (and prospective memory). The scheduled plan is interfaced with schema selection by the cognitive flexibility function. This function is the final interface between SAS and automatic processing.

Functional neuroimaging studies focused on procedural or implicit learning, i.e. when controlled processing becomes automatic, have revealed a change of brain activation during both motor and cognitive task learning. Specifically cortico-cortical and cortico-subcortical shifts of activation have been reported, with learning related decreases of activation in the prefrontal cortex and learning related increases in the motor, temporal and parietal cortex. In addition, the striatum appeared to play an important role, as it was involved in both automatic and controlled processing (Beauchamp et al., 2003; Debaere et al., 2004; Poldrack et al., 1999; Van der Graaf et al., 2004).

A neurodegenerative disorder that is characterized by a dysfunction of the striatum is PD. In PD impairments in both automatic and controlled processing have been reported. Specifically, PD patients show de-automatisation and implicit learning difficulties. In addition, there is a large literature about impaired executive functions in PD. SAS functions like monitoring, planning, set-shifting and divided attention are usually described under the

heading of executive functions (Dubois & Pillon, 1997). It is often tried to study these functions in isolation and various attempts to fractionate executive functions have been described (Cools et al., 2001; Dagher et al., 2001; Monchi et al., 2004; Weintraub et al., 2005a). According to Shallice & Burgess (1996), impairments in one of these executive functions might already lead to lacking cognitive (SAS) control. Looking at figure 4.1, this is easy to understand. For example, if the planning is deficient, it may be implemented perfectly, but the effect is poor.

Beginning with the case for automatic processing, we will review the evidence for impairments in automatic and controlled processing described in PD.

4.3 Automatic behavior

Automatic behavior can be applied in routine situations for which a dominant schema is available. PD has been described as a de-automatisation disorder (Saling & Phillips, 2007) and a good example of diminished levels of automaticity in the motor domain in PD is a decreased stride length when walking. To compensate patients must think about each step if they are to make adequately long steps, otherwise their steps become small (Wu & Hallett, 2005). Also imagining movements is impaired in PD, being specifically slowed at the most affected side of the body (Cunnington et al., 2001). This suggests that both the execution of movement as well as the motor plan are impaired. In addition, simulating movement with the most affected hand revealed enhanced activity in the right extra striate body and occipito-parietal cortex, suggesting an increased dependence on visual information during the generation of motor plans in PD (Helmich et al., 2007). Dual task performance, i.e. performing a routine task besides an other task, was also impaired in PD, partly due to diminished levels of automaticity according to (Wu & Hallett, 2007). PD patients thus appear to show de-automatisation in the motor domain. Studies focused on language production indicate that PD patients may also show decreased levels of automaticity in the cognitive domain, as PD patients relied more on executive functions when performing language tasks (Colman et al., 2008).

An fMRI study focused on achieving automatic movements in PD, reported that PD patients achieved automaticity with difficulty. Moreover, compared to healthy controls, PD patients showed increased activity in the cerebellum, premotor area, parietal cortex, precuneus and prefrontal cortex while performing automatic movements (Wu & Hallett, 2005), whereas no activation in the striatum was found. Instead PD patients kept activating cortical areas more which suggests difficulties achieving automaticity. This suggests that the expected shift from cortical to subcortical areas when controlled processing shifts

towards automatic processing, does not take place normally in PD patients due to the striatal dopaminergic dysfunction. It appears that in PD skill learning remains on the cognitive level while the more implicit procedural learning which should follow in the course of automatization does not occur sufficiently.

Several authors have reported that PD specifically show deficits in learning new procedures or habits, (Myers et al., 2003; Swainson et al., 2000), which is increasing with the development of the disease and is suggested to be independent of other cognitive impairments in PD (Muslimovic et al., 2007). Recently, it was reported that PD patients specifically show difficulties performing feedback-based learning tasks, while they perform equally compared to healthy controls on learning tasks without feedback (Shohamy et al., 2004).

Levodopa, which is often prescribed in PD, appears to influence feedback-based learning. Shohamy et al. (2006) reported that PD patients who used levodopa showed impaired feedback-based learning, while PD patients who did not use levodopa performed as well as healthy controls on the same task. The limbic or mesocorticolimbic circuit, which connects the ventral striatum to the orbitomedial prefrontal and limbic cortex (see figure 1.1) plays an important role in feedback based learning. This circuit is innervated by the VTA, which in the early stages of the disease shows a dopaminergic depletion to a lesser extent than the SN. Thus the VTA is relatively intact. A consequence is that the use of levodopa can overdose this nucleus, which may cause feedback based learning deficits (Cools, 2006). These findings can be further differentiated by Frank et al. (2004). They showed that PD patients who did not use levodopa showed a better performance when implicit learning was based upon negative feedback, i.e. patients learned to avoid stimuli which previously resulted in punishment. PD patients who did use levodopa, on the other hand, showed a better performance when implicit learning was based upon positive feedback, i.e. patients learned to react to previously rewarding stimuli. In a later publication Frank (2005) proposed a theory that might explain these reported differences between PD patients on and off levodopa. Dopaminergic neurons fire in response to rewarding feedback and the level of dopamine normally decreases in these neurons when confronted with negative feedback (Schultz, 2001). In this way a reaction in response to rewarding stimuli is stimulated and reactions in response to punishing stimuli are inhibited. PD patients who do not use levodopa show a constant lack of dopamine. Consequently patients are able to inhibit their response in reaction to punishing stimuli, while their response in reaction to rewarding stimuli is not stimulated. Hence, they learn better based upon punishing feedback (Frank, 2005). In contrast, PD patients who do use levodopa show a relatively increased level of dopamine in their brain. In these patients the level of dopamine in neurons can not decrease

in response to punishment, while their response to rewarding stimuli is stimulated. Patients on levodopa are consequently better capable of learning based upon rewarding feedback (Frank, 2005).

Thus, PD patients show difficulties applying and achieving automaticity. The latter could be due to an inability to shift from cortical to subcortical areas when information processing becomes more automatic. Specifically, PD patients show deficits when implicit or procedural learning was based upon feedback, which in turn is influenced by the use of levodopa: PD patients who do not use levodopa, learn by avoiding negative stimuli due to a lack of dopamine in their brain, while PD patients on levodopa, learn by responding to rewarding stimuli due to a relatively overdose of dopamine in the limbic or mesocorticolimbic circuits.

Focusing on the mental schema framework (figure 4.1) this suggests that PD patients show deficits developing a dominant schema, which is especially present in situations in which patients receive feedback during learning. Since it has been shown that learning deficits in PD are not associated with executive impairments (Muslimovic et al., 2007) and PD patients eventually do achieve automaticity, it can be suggested that learning impairments in PD are specifically due to a difficulty shifting from controlled to automatic processing, which in turn is due to an inability to shift from cortical to subcortical areas.

4.4 Controlled behavior

Executive dysfunctions are the most common cognitive impairment in non-demented PD patients and although memory and visuospatial dysfunction have been reported, it was argued that these are secondary to executive dysfunctions in PD (Dubois & Pillon, 1997). As described above executive functions can be viewed as a set of subprocesses of the SAS (see figure 4.1). In PD deficits in several of the subprocesses of cognitive control (SAS) have been proposed.

A central subprocess of cognitive control (SAS) is the selective phasic modulation (facilitation and inhibition) of schemata. The efficiency of this process is assessed with tests of mental flexibility, in which subjects must rapidly switch between different approaches to a problem or task. Many studies report decreased flexibility or set-shifting impairments in PD (Cools et al., 2001; Green et al., 2002; Muslimovic et al., 2005), being already present in the early stages of the disease and in PD patients who do not yet receive anti-parkinson medication (Muslimovic et al., 2005).

Set-shifting deficits are thought to be specifically present when interference of competing tasks sets is present and are hypothesized to be due to dysfunctional selection mechanisms, necessary for disengaging from a previous task set and engaging a new task set in the face of distraction (Cools et al., 2001). Levodopa, a dopamine precursor that is metabolized into dopamine after crossing the blood-brain-barrier, leading to increased levels of dopamine in the brain, can alleviate set-shifting deficits in PD (Cools et al., 2003).

Neuroimaging studies focused on set-shifting reported that healthy controls showed fronto-striatal activity, involving a co activation of the mid-ventrolateral prefrontal cortex and caudate nucleus, when receiving a signal that a shift was needed (Monchi et al., 2001). PD patients, on the other hand, showed no activation in this fronto-striatal circuit when a mental shift was needed. Instead, PD patients showed increased dorsolateral prefrontal cortex activation, which was not co activated with the striatum (Monchi et al., 2004). This suggests that PD patients compensate for the dopaminergic dysfunction of the fronto-striatal circuits and rely more on prefrontal areas for set-shifting, implying cortico-cortical and subcortical-cortical shifts.

Before the selection and adjustment of schemata a plan must be made on how to reach a goal. Planning impairments have been described in PD in the early stages of the disease and also in patients who do not yet use anti-parkinson medication (Muslimovic et al., 2005; Schneider, 2007; Weintraub et al., 2005a). The fronto-striatal circuits are involved in planning (Monchi et al., 2006) and using a planning task during $H_2{}^{15}O$ – Positron Emission Tomography (PET), Dagher et al. (2001) showed associations between activity in prefrontal areas, anterior cingulate cortex and the complexity of the task in both healthy controls and PD patients. In addition, an association between task complexity and activation in the right dorsal caudate nucleus in healthy controls was reported, while no such association was found in PD patients. This also suggests that PD patients used more cortical areas for planning, while healthy controls relied on the fronto-striatal circuits.

According to the mental schema framework (figure 4.1), a plan is based on declarative knowledge on how to obtain a goal and on the amount of effort that is invested. Also in these two subprocesses impairments have been proposed in PD patients.

Declarative memory is our personal and world knowledge we have conscious access to. Studies by Green et al. (2002) and Muslimovic et al. (2005) report that PD patients are impaired in recalling information from declarative memory. On the other hand, PD patients, do show enhanced hippocampal activity during a planning task, suggesting that PD patients relied more on their declarative memory during planning than healthy controls (Dagher et al., 2001) even though this may be impaired.

To make a plan for a novel situation not only declarative knowledge is required but also mental effort must be invested. In clinical settings it was noticed that PD patients often needed encouragement to complete a task, which has been interpreted as a capacity limitation with regard to mental effort (Lees, 1992).

When performing a planning task PD patients solved fewer of the most difficult planning puzzles and made fewer attempts to solve the planning puzzles than healthy controls, suggesting a difficulty in sustaining adequate mental effort (Schneider, 2007).

A factor that might influence sustained effort is fatigue, a common problem in PD affecting 33 to 58% of patients (Friedman et al., 2007). Although, the influence of fatigue on cognition in PD has not been directly investigated, an association between fatigue and hypoperfusion of the frontal lobe was found (Abe et al., 2000), suggesting that fatigue might have a negative influence on cognition in PD patients.

Thus, planning performance in PD patients may be negatively influenced by impaired recall from declarative memory and decreased effort or fatigue.

During and also after the formation of a plan and the selection and manipulation of schemata, information needs to be kept active in working or prospective memory. Reduced working memory capacity has been frequently reported in PD, specifically when manipulation of information is required (Green et al., 2002; Muslimovic et al., 2005). The involvement of the fronto-striatal circuits in working memory is confirmed by Lewis et al. (2003) who used a working memory paradigm during functional Magnetic Resonance Imaging (fMRI) and showed signal intensity reductions in the striatum and frontal cortex in cognitively impaired PD patients compared to cognitively intact PD patients. Concerning prospective memory, studies report that PD patients specifically show prospective memory deficits when stressed to focus on an ongoing task (Altgassen et al., 2007). These are however thought to be due to a reduced working memory capacity (Altgassen et al., 2007; Kliegel et al., 2005). This indicates that working memory impairments are a central memory impairment in PD.

The monitor is also a central subprocess of the SAS. As described above, it screens ongoing behavior and when it receives emotional or motivational information, the monitor activates the upper half of the model depicted in figure 4.1. The emotional and motivational information is based upon context and content aspects of a stimulus and can in turn also influence these aspects of the stimulus. Decreased levels of motivation have been reported in PD (Aarsland et al., 2005). Furthermore, it has been suggested that PD patients show

diminished novelty seeking (Kaasinen et al., 2001; Tomer & Aharon-Peretz, 2004), i.e. a diminished tendency toward 'intense exhilaration or excitement in response to novel stimuli, cues for potential rewards or potential relief of punishment' (Cloninger, 1987). Emotional information processing deficits have also been reported in PD patients, especially concerning non-verbal emotional information (Dujardin et al., 2004a), which could be a behavioral complication of bilateral subthalamic nucleus deep brain stimulation (STN-DBS), one of the treatment methods of PD (Dujardin et al. (2004b); see below for a description of STN-DBS).

PD patients can thus be less likely to activate the upper half of the model, due to decreased motivation, a diminished novelty seeking and a diminished non-verbal emotional processing. Whether PD patients show a diminished monitoring function itself is hard to determine, since the monitor is a subprocess which is difficult to conceptualize. A suitable task for this purpose could be the Six Elements Test of the Behavioral Assessment of the Dysexecutive Syndrome (Wilson et al., 1996) which requires a comprehensive view over future and ongoing behavior. This task or anything similar was however, according to our knowledge, not applied in PD.

A subprocess which can influence both controlled and automatic processing and that can stop an ongoing response is inhibition. Inhibition deficits have been reported in PD and are especially present after STN-DBS (Hershey et al., 2004; Schroeder et al., 2002). STN-DBS consists of implanting electrodes in the STN, which is part of the fronto-striatal circuits (see figure 1.1) and plays a prominent role in the pathophysiology of PD. It shows increased excitatory activity in PD, which consequently leads to a reduced activation of the thalamus and prefrontal cortex, eventually leading to the development of akinesia, bradykinesia, bradyphrenia and cognitive deficits in PD. It has been hypothesized that applying STN-DBS causes a release of the "brake" on the cortical areas and has been shown to improve motor symptoms (Esselink et al., 2004; Herzog et al., 2003; Portman et al., 2006). The influence of STN-DBS on cognitive function however, is more complicated (Smeding et al., 2006). According to Frank et al. (2007) the STN normally provides a control signal in decision conflicts (am I going left or right?), temporarily preventing the execution of any response. Due to STN-DBS PD patients show speeded responses in conflict situation, i.e. they show a decreased ability to inhibit a response in decision conflicts. This is confirmed by Hershey et al. (2004) who showed that STN-DBS reduced response inhibition under conditions of greater challenge to cognitive control and Smeding et al. (2006) who showed decreased performance on the Stroop task in PD patients on STN-DBS. Moreover, it was reported that STN-DBS decreases regional cerebral blood flow in the anterior cingulate

gyrus and ventral striatum during the Stroop task and impaired task performance at the same time (Schroeder et al., 2002).

Thus, PD patients who are not on STN-DBS are able to inhibit responses, since the increased excitatory activity of the STN causes reduced activation of the thalamus and prefrontal cortex. On the other hand, STN-DBS causes a release of the "brake" on cortical areas in PD patients and consequently a decreased ability to inhibit responses.

In conclusion, PD patients show executive dysfunctions due to deficits in many different subprocesses of cognitive control (SAS): cognitive flexibility, planning, declarative and working memory, effort, motivation, emotional processing and inhibition. Neuroimaging studies focused on cognition in PD showed decreased activation of the fronto-striatal circuits and increased activation of the prefrontal cortex. This suggests that PD patients show increased cognitive control, using more frontal areas for cognitive tasks which indicate compensatory mechanisms reflected by cortico-cortical and subcortical-cortical shifts. The use of levodopa can alleviate cognitive deficits in PD, however the influence of levodopa on different cognitive functions, i.e. subprocesses of cognitive control (SAS) was not investigated. STN-DBS, an other treatment strategy applied in PD, improves motor symptoms. However, the influence of STN-DBS on cognitive functions is more complicated and has been shown to have a negative influence on inhibition. Thus, impairments in cognitive control or the executive functions in PD appear to be the result of the complex interplay between the dopaminergic dysfunction of the fronto-striatal circuits and treatment strategies.

With regard to the comprehensive mental schema framework an other explanation for the impairments within cognitive control or executive functions, besides the explanation of impairments in different subprocesses, needs to be added. Within the comprehensive mental schema framework (see figure 4.1; Brouwer & Schmidt (2002)) the dynamic relations between the subprocesses of automatic and controlled processing are reflected. Considering this framework, the increased reliance on cognitive control in PD suggests that the regulation of behavior shifts from automatic to controlled processing. This is consistent with deautomatisation and implicit learning impairments in PD patients as described above. The shift from automatic to controlled processing however, indicates that if there is something wrong with automatic information processing this will also affect controlled processing, suggesting that impairments in the subprocesses of controlled processing are secondary to impairments in automatic processing. The strongest evidence for impairments in controlled processing in PD will therefore be studies that control for confounding

influence of impaired automatic processing and other subprocesses of controlled processing (see figure 4.1). The problem with tests used to assess the cognitive functions in PD however, is that they not only assess the cognitive function they declare to measure but also many other cognitive functions, such as implicit learning, working memory and visuospatial functions. For example, the Odd man out test (Flowers & Robertson, 1985) requires both the implicit learning of rules and cognitive flexibility (Cools et al., 2001). According to our knowledge, only Cools et al. (2001) studied cognition in PD controlling for confounding influences. They reported cognitive flexibility impairments in PD, which were specifically present when the load on selection mechanisms increased. PD patients thus show genuine cognitive flexibility impairments. Future research should be focused on unraveling which cognitive impairments are specific for PD. Specifically it needs to be determined to what extent impairments in controlled processing are secondary to impairments in automatic processing.

4.5 Conclusion

PD patients show automatic processing deficits. They show deautomatisation and achieve automaticity with difficulty. Moreover, PD patients specifically show deficits when learning is based upon feedback, that in turn is influenced by the use of levodopa. Furthermore, PD patients do not show a shift of activation from cortical to subcortical areas when controlled processing becomes rather automatic, which has been observed in healthy controls. Instead, PD patients activate more cortical areas. This suggests a compensatory mechanism, not reflected by a shift of activation from cortical to subcortical areas but by a maintenance of activation in cortical areas.

In addition, PD patients show impairments in cognitive control or executive functions, described as deficits in many different subprocesses of the SAS: cognitive flexibility, planning, declarative and working memory, effort, motivation, emotional processing and inhibition. These are to a large extent the consequence of the dopaminergic dysfunction of the fronto-striatal circuits. PD patients compensate for this dysfunction by showing increased prefrontal activation, implying cortico-cortical and subcortical-cortical shifts of activation. Whether these compensatory mechanisms cause an increased performance level is not clear. If this was the case it might partially explain why not all PD patients show executive impairments. Moreover, it is also unknown whether all PD patients compensate and how these compensatory mechanism develop with the progression of the disease.

According to our mental schema framework, cognitive control (SAS) has its effect on behavior by modulating, facilitating or inhibiting schemata. If there is something wrong

with automatic schema-driven information processing, this will also effect the application of executive functions, suggesting that the executive impairments are secondary to automatic impairments. The strongest evidence for impaired executive functions will therefore be studies that control for the effects of impaired automatic information processing, for example by showing that the impairments can be dissociated.

In conclusion, the cognitive impairments observed in PD, both at the level of controlled and automatic processing, are the result of a complex interplay between the dopaminergic dysfunction of the fronto-striatal circuit, compensatory mechanisms and treatment strategies applied in PD. Future research should focus on the influence of automatic processing impairments on cognitive control and on the compensatory mechanisms.