Chapter 7

Controlled behavior in Parkinson's disease: initiative, planning and multi-task performance

Janneke Koerts, Marije van Beilen, Klaus L. Leenders & Wiebo H. Brouwer

Submitted

7.1 Abstract

Starting from a comprehensive schema model of cognitive control and executive functions, initiation of behavior, everyday planning and multi-task performance was studied with the Cognitive Effort Test (CET). The CET is a relatively unstructured multiple component visual motor task from which three variables are derived, Initiative, Planning and Multi-task performance.

Forty non-depressed PD patients, with a mild to moderate disease severity, and 34 healthy controls of similar age, gender and education were included in this study. All were assessed with the CET and a subgroup of PD patients (n=28) and healthy controls (n=19-20) was also assessed with tests for more elementary executive functions and psychomotor speed. In addition, the severity of motor symptoms, the use of antiparkinsonian medication, apathy and fatigue were assessed in all patients.

Despite the expectation of impairments in initiating behavior in PD patients no difference was found between PD patients and controls with regard to Initiative. Planning was different however; the groups engaged in planning equally often, however PD patients tended to plan sequential task performance, while healthy controls tended to plan simultaneous task performance. In the PD patients psychomotor speed was an important determinant in the planning of how to perform multiple tasks. The associations with performance on tests of executive functions, motor severity, apathy and fatigue were however negligible. Besides the intention to perform tasks sequentially, PD patients also actually performed the multiple tasks sequentially, instead of simultaneously. This tendency to work sequentially was significantly predicted by a decreased cognitive flexibility.

In conclusion, PD patient did not show impairments in initiating behavior compared to healthy controls. They did however, tend to plan sequential, instead of simultaneous task performance. This difference in planning does not indicate a specific impairment of planning but rather reflects a compensation for a decreased psychomotor speed. In addition, PD patients also actually performed tasks sequentially instead of simultaneously. This ‘choice’ appeared to be significantly influenced by a decreased attentional flexibility.

7.2 Introduction

Parkinson's disease (PD) is a neurodegenerative movement disorder characterized by a dopaminergic dysfunction of the striatum. The striatum is extensively connected with the prefrontal cortex through the frontostriatal circuits (see figure 1.1), which are functionally impaired as well in PD (Alexander et al., 1986). Motor symptoms are the clinical hallmark, however non-motor symptoms are often present. Cognitive impairments in the domain of the executive functions are frequently observed (Dubois & Pillon, 1997).

Executive functions and cognitive control play an important role in non-routine situations. Controlled processing concerns deliberate planning and regulation in situations where current schemata are not sufficient. It involves inhibition of automated responses, retrieval from declarative memory, planning and regulation. The complex cognitive function that is described to regulate controlled processing is the Supervisory Attentional System (SAS; Norman & Shallice, 1986), which is closely tied to the prefrontal cortex. To be able to control behavior the SAS is assumed to have a number of constituent more elementary functions, like monitoring, planning, set-shifting 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 are depicted in figure 4.1 (adapted from Brouwer & Schmidt (2002)).

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. 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 risks by the monitor function. If a challenge to important (biological) goals is sensed, ongoing behavior is inhibited and the SAS is switched on further. Motivated by the need to realize an 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 set-shifting function, which is the final interface between the SAS and automatic processing.

In PD impairments of working memory, planning, cognitive flexibility and generating new rules have been reported (Cools et al., 2001; Monchi et al., 2004; Muslimovic et al., 2005). PD patients also show difficulties initiating behavior especially when they have to internally generate behavior, while they do not show decreased levels of performance when confronted with external cues (Georgiou et al., 1994; Rubinstein et al., 2002). The

difficulties of internally generating behavior may be related to apathy and fatigue, which can be present in PD, even in the absence of depression (Alves et al., 2004; Kirsch-Darrow et al., 2006). Besides these impairments in the more elementary executive functions, PD patients can also show a decreased psychomotor speed or bradyphrenia. Thus, in PD an impairment of the SAS is likely to emerge, caused by impairments in more elementary (executive) functions.

Executive functioning and cognitive control needed in daily life is difficult to assess and patients with frontal lobe lesions and impairments in executive functioning in daily life do not all show a decreased performance on the tests for executive functions (Shallice & Burgess, 1991). These tests are often structured and offer a method: rules are explained, goals are set and behavior is prompted and stopped (Manchester et al., 2004). In addition, these tests are often aimed at isolating one aspect of the executive functions, such as inhibition or set-shifting, in order to measure that aspect reliably and excluding other influences. Executive functioning in daily life however, requires a collaboration between the many different aspects of the executive functions (see figure 4.1), without a structured method being offered. A good example of a daily life situation in which executive functioning and cognitive control is needed is multi-tasking, e.g. walking and talking. Studies reported that PD patients show dual-task impairments (Brown & Marsden, 1991). The general picture emerging from these studies is that the performance on a primary tasks deteriorates when a secondary tasks needs to be performed, with increased deterioration when the secondary task was more demanding (Bloem et al., 2006).

The aim of this study is to investigate executive functioning in non-depressed PD patients, with a mild to moderate disease severity, specifically focusing on the initiation of behavior, everyday planning and multi-tasking. For this purpose the recently developed Cognitive Effort Test (CET; Van Beilen et al. (2005)) was used. This test is a relatively unstructured multiple component visual-motor task from which three variables are derived, initiative, planning and multiple task performance. In addition, it will be investigated to what extent the initiation of behavior, planning and multi-tasking of PD patients is influenced by more elementary executive functions (cognitive flexibility, inhibition, working memory) and by psychomotor speed, motor symptoms, use of antiparkinsonian medication, fatigue and apathy.

7.3 Methods

Subjects

40 PD patients participated in this study. All patients were diagnosed with idiopathic PD according to the criteria of the UK Parkinson's Disease Society Brain Bank. The patient group consisted of 19 men (47%) and 21 women (53%). In addition, 34 healthy controls were included in this study. This group consisted of 16 men (47%) and 18 women (53%). Level of education was rated for all participants with a Dutch education scale, ranging from 1 (elementary school not finished) to 7 (university degree). Groups did not differ in age (t=-1.54; p=0.13), gender (Chi-Square=0.00; p=0.97) and education level (Mann-Whitney U=540.00; p=0.15). In table 7.1 demographic and illness characteristics of PD patients and healthy controls are described.

Table 7.1 Demographic and illness characteristics of PD patients (n=40) and healthy controls (n=34)

	PD patients		Healthy controls	
	Mean (SD)	Range	Mean (SD)	Range
Age	61.2 (7.5)	47-77	58.8 (6.0)	46-70
Education	5.5 (0.9)	4-7	5.7 (0.9)	3-7
MADRS total	5.8 (3.8)	0-14	3.2 (3.0)	0-11
Disease duration	5.3 (5.2)	0-19		
UPDRS, part III	20.5 (9.4)	5-53		
LEDD	500.0 (445.4)	0-1512		

Exclusion criteria were neurological disorders other than PD and depression (MADRS < 15; Leentjens et al. (2000)). This study was approved by the medical ethical committee of the University Medical Center Groningen. All patients signed an informed consent prior to study inclusion.

Stimulus material and procedure

All participants were assessed with the CET and a subgroup of patients (n=20-28) and healthy controls (n=19-20) was assessed with tests of executive functions and psychomotor speed. In addition, the severity of motor symptoms, use of antiparkinsonian medication and symptoms of depression (including apathy and fatigue) of all patients were assessed. All patients were assessed in regular on-state.

Cognitive Effort Test (CET)

The CET (Van Beilen et al., 2005) is a multiple component visual motor task that provides participants with the goal to perform three tasks as accurately and as fast as possible, but does not offer a structured method that prompts participants to certain behavior. This test is focused on assessing the initiatives taken by participants, whether and how participants plan to perform the three tasks (sequential or parallel) and how participants actually perform the three tasks. Each participant can voluntarily decide how many tasks he can handle simultaneously to complete the CET successfully.

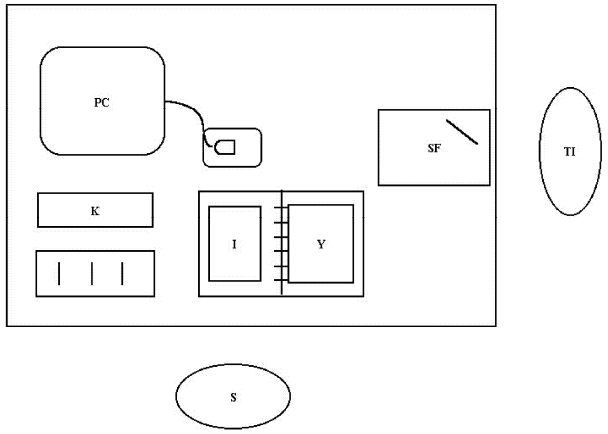
The CET was developed due to the low ecological validity of many available tests. Previously, it was successfully applied in Schizophrenia patients and healthy controls and appeared to be a better predictor for group membership than existing tests for executive functions, such as the Wisconsin Card Sorting Test (Van Beilen et al., 2005).

The CET consisted of the following three tasks:

1. The Computer: when started by the participant the computer task runs itself for 2 minutes during which the participant has to wait before being able to continue. This information is explicitly mentioned in the instruction and is visible, by means of a timeline, on the computerscreen. At the end of the first minute a password is asked unexpectedly. Participants are not instructed what to do and need to show the initiative to ask the test instructor for the password. They can also make up a password themselves, there is however only one correct password. At the end of the second minute participants are instructed by a message on the computer screen to type the alphabet. After this the task is finished, regardless whether any mistakes were made.
2. The Yellow pages: this task requires the full visual attention of the participant. Five telephone numbers of different companies must be looked up in the yellow pages and spoken out loud.
3. The Screws: three nuts need to be threaded up and down three large fixed screws. This a simple motor task, which can be done by either the left or the right hand. It is important to notice that the board to which the screws are attached, has a 8 cm high backwall attached to it.

These tasks are placed in front of the participants is such a way that they allow several initiatives (e.g. moving the screwboard, which is blocking the keyboard due to the high backwall, or moving the keyboard; see figure 7.1). Participants are provided with a summary of the instruction in order to be able to check the instructions during the test without having to rely on memory.

Figure 7.1 Placement of tasks of CET



Legend: PC – Monitor PC; K – Key board; III – Screw task; I – Instruction Form; Y – Yellow pages; SF – Scoring Form; S – Subject; TI – Test Instructor.

Instructions: Participants are informed about the tasks and are instructed to complete them as fast and as accurately as possible. Although it is mentioned that they are allowed to do several tasks at the same time, they are not explicitly instructed to do so. Nothing is said about the password or the movement of material. After completing the instructions, the test instructor leaves the room for 1 minute with an excuse (i.e. searching for the summary instruction form), and after he returns participants are asked how they plan to do the test.

Three summary scores are computed:

1. Initiative: The participants are rated with regard to the following six initiatives: asking for the password, making up a password themselves, consulting the instruction form, moving the screwboard, moving the keyboard and showing any other initiative during the test (e.g. talking to the test instructor). Each initiative is rated with one point so that a maximum of six points can be obtained.
2. Planning: When the test instructor leaves the room participants have the opportunity to form a plan without being prompted to do so. The participants receive one point when a plan was made. Also the quality of the plan is rated. The participants receive no points when they have planned to do one task at a time, one point when they have planned to do two tasks at the same time and two points when they have planned to do three task simultaneously.

3. Multi-tasking: In order to calculate a multi-tasking score it is important to determine if participants performed the three (or two or one) tasks simultaneously when they had the opportunity to perform the three (or two or one) tasks simultaneously. Therefore three stages are defined and the proportion of time spent on working on multiple tasks is rated:
    I. In the first stage it is possible to work on three subtasks. This stage starts when the test is started and ends when the subject has completed the first task. The proportions of time working on one, two or three tasks simultaneously during this stage are rated, adding up to 100%.
    II. In the second stage one task is finished and two still need to be worked on. The proportion of time working on one or two tasks during this stage is rated, adding up to 100%.
    III. In the third stage two tasks are finished and 100% is spent on working on one task.

    Subsequently, the total proportion of time spend on one, two or three tasks is calculated by adding the time spent on one, two or three tasks during these different stages. This however, results in a possible maximum score of 100% working on three subtasks, 200% working on two tasks, and 300% working on one task at the same time. If these scores would simply be combined, the proportion of time worked on one task has a stronger weight than the proportion of time working on two or three tasks, so an adjustment is needed to make the scores comparable. Therefore, the total proportion of time working on two tasks is divided by 1,5 and the total proportion of time working on one task is divided by 3. Finally, these scores are added, which results in a summary score between 100% and 200%. A higher score means that participants have performed more tasks simultaneously. An example of this calculation is given in table 7.2.

<u>Elementary aspects of executive functions:</u>

- Inhibition: The Stroop Color Word Test (Stroop, 1935) was used to assess inhibition. This test contains three cards, the Word card, the Color card and the Color-Word card. The target measure for inhibition was the Color-Word card. This task requires patients to suppress the automatic tendency to read, while naming the color of words that are themselves color names. The performance was corrected for psychomotor speed, by dividing the time needed for the Stroop Color-Word card by the time needed for the Stroop Color card.

Table 7.2 Example of calculating Multi-tasking score

Total time CET:	260 s	
Stage 1		
Total time:	130 s	
Time 3 tasks:	0 s	0%
Time 2 tasks:	120 s	92.3%
Time 1 task:	10 s	7.7%
Stage 2		
Total time:	20 s	
Time 2 tasks:	0 s	0%
Time 1 task:	20 s	100%
Stage 1		
Total time:	110 s	
Time 1 task:	110 s	100%
Total 3 tasks:	0	0 points
Total 2 tasks:	(92,3 + 0)/1,5	61.53 points
Total 1 task:	(7,7 + 100 +100)/3	69.23 points
Total Multi-tasking:		130.76 points

- Cognitive flexibility: Cognitive flexibility was assessed with the Trailmaking Test (Reitan, 1958) and Odd Man Out (Flowers & Robertson, 1985). The Trailmaking Test consists of two parts. Part A requires patients to draw a line, as fast as possible, between numbers (1-25) in ascending order. In part B numbers and letters are used and patients need to switch attention between both concepts: they have to draw a line between both types of stimuli in ascending order, alternating between numbers and letters and also as fast as possible. The target measures for cognitive flexibility were the performance on part B (this part is not corrected for psychomotor speed) and the performance on part B divided by the performance on part A, the so-called B/A index which is corrected for psychomotor speed.

  The Odd Man Out requires patients to indicate which shape, of a set of four shapes, is different. Three selection rules are possible. Two sets of twelve cards are used. For each set patients have to specify a different rule. Subsequently, both sets of cards are alternated four times and the total number of incorrect responses are rated.
- Working memory: The digit span of the Wechsler Adult Intelligence Scale (Stinissen et al., 1970) was used to assess working memory. Patients had to repeat

a string of digits of increasing length. The test contains a forward and a backward condition. The total number of strings that was repeated correctly was rated.

Psychomotor speed: the time needed on Trailmaking A (Reitan, 1958), Stroop Word Card and Stroop Color Card (Stroop, 1935) were used to assess psychomotor speed.

Disease characteristics:

- The Unified Parkinson's Disease Rating Scale, part III (Fahn et al., 1987), was used to assess motor symptoms of all patients.
- A Levodopa Equivalent Daily Dose (LEDD) score was calculated for all patients according to the following formula: levodopa dose (100 mg) x 1 (added with 0.2 x levodopa dose if using entacapone with each dose) + (slow release levodopa x 0.7) + bromocriptine x 10 + ropinirole x 20 + pergolide x 100 + pramipexole x 100 (Esselink et al., 2004).
- The Montgomery-Åsberg Depression Rating Scale (Montgomery & Asberg, 1979) was used to assess symptoms of depression: apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts and suicidal thoughts.

Statistical analyses

First, composite variables were formed for Tremor (UPDRS items 20, 21), Bradykinesia (UPDRS items 23, 24, 25, 26, 31) and Axial impairment (UPDRS items 27, 28, 29, 30). Since rigidity was measured by one specific UPDRS item (item 22), a composite variable was not formed for this motor symptom.

Normality of data was analyzed using the Shapiro-Wilk test and QQ-plots. Not all variables were normally distributed in both groups. Therefore, non-parametric tests were used to verify the results of the parametric tests. The results of the non-parametric tests supported our parametric findings, therefore only the results of the parametric tests are described.

Independent samples t-tests were used to compare PD patients and healthy controls on the scales of the CET. To determine whether PD patients and healthy controls differed with regard to the specific initiatives that were rated during CET performance, the percentages of PD patients and healthy controls showing certain initiatives were calculated and both groups were compared for each initiative using Chi-square. Concerning the Planning scale it was determined whether PD patients made a plan as often as healthy controls and whether

there were differences between groups concerning the quality of the plan, using independent samples t-tests. In addition, Pearson correlations were calculated within both groups between the performance on the Multi-tasking and Planning scale.

PD patients and healthy controls were also compared on all tests for executive functions and psychomotor speed. In addition, the performance of PD patients and healthy controls on the tests for executive functions and psychomotor speed were analyzed using methods which are used in clinical practice. Standard, and if possible percentile, scores were derived for each patient, using normative samples of healthy subjects, which have been determined for several neuropsychological test (Stroop (Schmand et al., 2003), Trailmaking test (Schmand et al., 2003), Odd Mann Out (Pomati et al., 1996), Digit span (Stinissen et al., 1970)). All normative data sets included a correction for age and when relevant a correction for gender and level of education. Cognitive impairment on a test was defined as a performance equivalent to the performance of the worst 10% of the normative sample, i.e. 90% of healthy subjects (of the same age and when relevant of the same gender and level of education) performed better on the cognitive test.

In addition, one-tailed (based on previous literature (Brown & Pluck, 2000)) Pearson correlations were calculated between the performance on the CET scales and standard percentile scores for the performance on tests for executive function, psychomotor speed (a composite variable based on Stroop word and color card and Trailmaking A), apathy (MADRS item 8), fatigue (MADRS item 7), the severity of motor symptoms (tremor, bradykinesia, axial impairment and rigidity) and the use of antiparkinsonian medication (LEDD score).

7.4 Results

PD patients and healthy controls did not differ on the Initiative scale of the CET (see table 7.3). However, concerning the specific initiatives that were rated it was found that PD patients did not make up a password themselves as often as healthy controls. With regard to the other initiatives that were rated no differences were found between groups (see table 7.4). PD patients scored significantly lower on the Multi-tasking scale of the CET than healthy controls and a trend to a difference was found for the Planning scale of the CET (see table 7.3). More specifically, PD patients made a plan as often as healthy controls (t=-0.30; p=0.38), however PD patients scored significantly lower on the quality of the plan than healthy controls (t=2.64; p=0.01), which means that they planned to do fewer task simultaneously than healthy controls. A significant association between Multi-task

performance and the quality of the plan was found within PD patients (r=0.60; p<0.005) and healthy controls (r=0.68; p<0.005). The variable 'quality of the plan' was used in further calculations.

Table 7.3 Cognitive Effort Test scores of PD patients (n=40) and healthy controls (n=34; one-tailed)

	PD patients M (SD)	Healthy controls M (SD)	t	p
Initiative	2.73 (1.15)	2.97 (1.24)	0.88	0.19
Planning	1.45 (0.78)	1.76 (1.02)	1.50	0.07
Multi-tasking	128.80 (22.06)	141.26 (24.39)	2.31	0.01

Table 7.4 The percentage of Healthy Controls (n=34) and PD patients (n=40) that showed initiatives including a comparison of these groups using Chi-square (one-tailed)

	Healthy Controls	PD	Chi-square	p
Asking password	91	98	1.50	0.11
Making up password	21	2	6.43	0.01
Consulting instruction form	41	49	0.43	0.26
Moving screwboard	77	66	1.01	0.16
Moving keyboard	27	15	1.63	0.10
Other initiatives	32	29	0.08	0.39

The comparison of PD patients and healthy controls for the performance on the different tests for executive functions and psychomotor speed showed that PD patients scored significantly lower on the Odd man out test (cognitive flexibility), Trailmaking B (cognitive flexibility and psychomotor speed) and Trailmaking A (psychomotor speed). Trends to differences between PD patients and healthy controls were found for Stroop interference index (Inhibition) and Stroop color card (psychomotor speed). On all other tests no significant differences were found between PD patients and healthy controls (see table 7.5).

In addition, a more clinical approach was used by comparing the performance of PD patients to normative samples of the same age (and when relevant of the same gender and with the same level of education). PD patients showed the highest frequency of impairment on the Trailmaking A (29%), Stroop word card (25%) and Stroop Color card (21%), Trailmaking B (14%) and Inhibition (7%). On the Odd man out, Trailmaking B/A and Digit span none of the PD patient showed a score that was clinically significant (see table 7.5).

The correlational analyses showed that within PD patients the Initiative scale of the CET was not associated with the performance of the different tests for executive functions and psychomotor speed, apathy, fatigue, motor symptoms or the use of antiparkinsonian

medication (see table 7.6). Planning and Multi-tasking were, on the other hand, both positively correlated with Trailmaking B and psychomotor speed. In addition, Planning was positively correlated with the use of antiparkinsonian medication (LEDD score; see table 7.6).

Table 7.5 Performance of PD patients (n=40) and healthy controls (n=34) on tests for more elementary executive functions and psychomotor speed (one-tailed)

	PD patients			Healthy controls				
	M (SD)	n	%*	M (SD)	n	%*	t	p
Inhibition	1.63 (0.33)	28	7	1.50 (0.22)	19	0	-1.58	0.06
Cognitive flexibility								
- Odd man out	3.86 (4.95)	28	0	1.20 (2.02)	20	0	-2.60	0.01
- Trailmaking B/A	2.17 (0.44)	28	0	1.95 (0.77)	19	5	-1.04	0.15
- Trailmaking B**	102.79 (41.27)	28	14	70.20 (24.37)	20	5	-3.43	0.00
Working memory	13.00 (3.21)	28	0	14.45 (4.71)	20	0	1.02	0.16
Psychomotor speed								
- Trailmaking A	48.43 (19.54)	28	29	37.55 (13.83)	20	10	-2.26	0.01
- Stroop Word Card	49.07 (11.15)	28	25	49.75 (12.97)	20	40	0.19	0.42
- Stroop Color Card	63.29 (13.97)	28	21	58.45 (9.45)	20	10	-1.43	0.08

* % of impaired participants compared to a normative sample

** This variable is not corrected for psychomotor speed

Since Trailmaking B and psychomotor speed (Trailmaking A, Stroop word and color card) were partly assessed with the same test the possibility existed that these variables showed high intercorrelations. Consequently one variable could have been a third variable in the association between an other variable and the CET scales. Therefore two stepwise regression analyses were performed. The first included Planning (i.e. the quality of the plan) as the dependent variable and Trailmaking B and psychomotor speed as predictors. This analysis showed that psychomotor speed explained 25% of variance ($F=7.15$, $p=0.01$). Trailmaking B was not entered into this regression model. The second analysis included Multi-tasking as the dependent variable and Trailmaking B and psychomotor speed as predictors. This analysis showed that Trailmaking B explained 33% of variance ($F=12.80$, $p=0.00$). Psychomotor speed was not entered into the regression model. Trailmaking B assesses both cognitive flexibility and psychomotor speed. The finding that Multi-tasking was significantly predicted by Trailmaking B may therefore have been influenced by psychomotor speed. To correct for this a partial correlation was calculated between Multi-tasking and Trailmaking B, controlling for psychomotor speed. This analysis showed that Multi-tasking and Trailmaking B were significantly associated ($r=0.36$; $p=0.03$).

Table 7.6 Associations between tests for more elementary executive functions, psychomotor speed, motor symptoms, medication use, apathy, fatigue and CET scales within PD patients (n=40; one-tailed)

	Initiative r	Planning*** r	Multi-tasking r
Cognitive flexibility			
- Trailmaking B	-0.25	0.44*	0.57**
- Odd man out	-0.29	0.24	0.18
Inhibition	-0.20	0.00	-0.18
Psychomotor speed	-0.04	0.50**	0.54**
Apathy	-0.11	0.11	-0.06
Fatigue	0.26	-0.02	0.25
Motor symptoms			
- Tremor	-0.09	0.33	-0.06
- Bradykinesia	0.32	-0.26	-0.15
- Rigidity	-0.00	-0.05	-0.05
- Axial impairment	0.16	-0.29	-0.01
LEDD score	-0.08	0.48**	0.18

* $p \leq 0.05$

** $p \leq 0.01$

*** represents the variable 'quality of the plan'

7.5 Discussion

Starting from a comprehensive schema model of executive functions and cognitive control (see figure 4.1) the initiation of behavior, everyday planning and multi-tasking was investigated in non-depressed PD patients, with a mild to moderate disease severity. For this purpose the recently developed Cognitive Effort Test (CET; Van Beilen et al. (2005)) was used. This test is a relatively unstructured multiple component visual-motor task from which three variables are derived, Initiative, Planning and Multiple task performance. In addition, it was investigated to what extent the initiation of behavior, planning and multi-tasking of PD patients was influenced by more elementary executive functions (cognitive flexibility, inhibition, working memory) and by psychomotor speed, motor symptoms, use of antiparkinsonian medication, fatigue and apathy.

Interestingly, PD patients and healthy controls did not differ on the Initiave scale of the CET. Previous studies reported that PD patients show difficulties initiating behavior especially when they have to internally generate behavior (Georgiou et al., 1994; Rubinstein et al., 2002). It was therefore expected that PD patients showed a decreased number of initiatives relative to healthy controls. Looking more specifically however, at the

different initiatives that were rated it was found that PD patients did not show the initiative of making up a password themselves as often as healthy controls. Concerning all other initiatives no differences were found between PD patients and healthy controls. It is hard to explain why only a difference between groups was found for the initiative 'making up a password'. Common sense suggests that participants would ask for a password rather than making up a password themselves, which is hardly ever correct. Possibly PD patients were better able to inhibit this unlogical response than healthy controls, which is in line with the pathophysiological model of PD that indicates that symptoms such as bradykinesia and akinesia are caused by an increased inhibitory influence of the striatum on the thalamus and prefrontal cortex. Another explanation could be that the initiative of making up a password themselves was too demanding for PD patients and required more from cognitive resources than initiatives such as 'asking for a password'. These explanations remain however to be elucidated. In general it can however be concluded that PD patients did not show impairments in initiating behavior.

PD patients were also not hindered by their motor symptoms in showing initiatives. They moved the screwtask and keyboard as often as healthy controls and no associations were found between motor symptoms and the Initiative scale. Furthermore, it was expected that initiating behavior by PD patients was related to apathy and fatigue, which can be present in PD in the absence of depression (Alves et al., 2004; Kirsch-Darrow et al., 2006). However, no associations were found between the apathy, fatigue and the Initiative scale of the CET in PD patients. Fatigue and apathy were assessed with items of the MADRS and it is possible that these symptoms were not assessed thoroughly enough. However, it also possible that the patients included in this study were not apathetic or fatigued enough, causing a relatively small distribution of data. Future research should therefore focus on the initiation of behavior of PD patients with severe symptoms of apathy and fatigue. In addition, it would also be interesting to investigate whether the initiation of behavior is decreased in PD patients with severe motor symptoms.

Thus, despite the expectation that PD patients would show impairments in initiating behavior, no differences were found between non-depressed PD patients with a mild to moderate disease severity and healthy controls. With regard to the comprehensive schema model of cognitive control and executive functions (see figure 4.1), this suggests that the effort component, which represents the ability to initiate behavior and realize opportunities, is correctly functioning in non-depressed PD patients with a mild to moderate disease severity.

PD patients scored significantly lower than healthy controls on the Multi-tasking scale of the CET, and a trend to a difference was found on the Planning scale. Looking more specifically at the Planning scale it was found that PD patients made a plan as often as healthy controls, however the quality of the plan of PD patients (i.e. the number of tasks they plan to perform simultaneously) was significantly decreased compared to healthy controls. PD patients thus planned and performed fewer tasks simultaneously than healthy controls.

Planning impairments (Foltynie et al., 2004; Weintraub et al., 2005a) might explain the finding that PD patients planned to perform fewer task simultaneously, relative to healthy controls. However, it was also found that the planning of the number of tasks that would be performed simultaneously was significantly predicted by psychomotor speed, i.e. PD patients who were slower, planned to perform fewer tasks simultaneously. A decreased psychomotor speed or bradyphrenia is one of the main characteristics of PD and it is likely that planning to perform fewer tasks simultaneously is a wise strategy to deal with a decreased psychomotor speed. PD patients are most likely aware of being slower and cope with this by planning to perform tasks more sequential instead of parallel. This is in line with findings that PD patients show impairments when having to perform dual tasks (Bloem et al., 2006; Brown & Marsden, 1991) and suggests that the planning of sequential task performance is a compensatory strategy for a decreased psychomotor speed. With regard to the schema model depicted in figure 4.1 it can thus be suggested that the planning ability as such is functioning correctly. Instead, psychomotor speed appears to be a determinant in the planning of how multiple tasks are performed by PD patients.

PD patients also actually performed fewer task simultaneously. Moreover, planning and multi-tasking of PD patients were significantly associated. Thus when PD patients planned to perform fewer tasks simultaneously they also performed fewer tasks simultaneously. This suggests that the monitoring function (see figure 4.1) correctly attunes the plan and the eventual performance. Multi-tasking was significantly predicted by cognitive flexibility (Trailmaking B) within PD patients, even after correction for psychomotor speed, which might have influenced the performance on this test. No associations were found between inhibition, working memory and multi-tasking. Thus, PD patients who show a decreased cognitive flexibility perform task sequentially instead of simultaneously. A decreased cognitive flexibility has previously been reported in PD (Cools et al., 2001) and as a consequence PD patients may be unable to flexibly divide attention over several tasks and therefore may not be able to pay attention to several tasks simultaneously. Consequently, tasks are performed in a more sequential, instead of parallel manner by PD patients. This is consistent with previous reports that PD patients showed impairments in a selection

mechanism that is necessary for disengaging from a current task and engaging to a new task in the face of distraction (Cools et al., 2001). Also, these results are in line with previous findings that PD patients performed a task with multiple dimensions by showing exaggerated attention to some aspects of the task, while relatively neglecting other aspects (Bialystok et al., 2008).

Thus, a decreased cognitive flexibility appears to play an important role in the 'choice' of PD patients to perform multiple tasks sequentially instead of simultaneously.

Apathy and fatigue were also not associated with Planning and Multi-tasking. Probably, the above described explanations for not finding associations between apathy, fatigue and Initiative can also be applied to these findings. Planning was however positively associated with the use of levodopa, i.e. PD patients who used more levodopa, planned to perform more tasks simultaneously. Whether levodopa facilitated the planning ability is hard to determine, since PD patients on and off levodopa were not directly compared. Previous studies did report that levodopa can have both a positive and a negative effect on cognition in PD (Cools et al., 2003; Cools, 2006). Interesting future research should therefore be focused on CET performance in PD patients both on and off levodopa.

In conclusion, despite the expectation of impairments of initiating behavior, non-depressed PD patients with a mild to moderate disease severity, did not show impairments in initiating behavior compared to healthy controls. These patients however, did tend to plan sequential task performance, while healthy controls planned simultaneous task performance. This difference in planning does not indicate a specific impairment of planning but rather reflects a compensation for a decreased psychomotor speed. In addition, PD patients also actually performed tasks in a more sequential instead of parallel manner relative to healthy controls. This 'choice' appeared to be significantly influenced by a decreased cognitive flexibility. With regard to the comprehensive schema model of executive functions and cognitive control it can be suggested that the planning and performance of multiple tasks is not influenced by impairments initiating behavior (effort) or a decreased monitoring function, since PD patients perform what they plan. Also, working memory and inhibition impairments did not play a role. Psychomotor speed, one of the more basic information transformation processes (see figure 4.1) and a decreased cognitive flexibility did however influence the planning and performance of multiple tasks. Based on these findings it can be hypothesized that a decreased psychomotor speed is an important determinant in the executive functioning in daily life of PD patients. It plays a role in the planning on how to handle multiple tasks. This plan and a decreased cognitive flexibility subsequently

determine that tasks are performed sequential instead of simultaneous by PD patients (see figure 7.2).

Figure 7.2 Multi-task performance in PD patients