

Training of executive functions in Parkinson's disease

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Abstract

Cognitive disturbances are common in Parkinson's disease (PD). Examination of cognitive function often reveals deficits in executive functions, including maintenance and inhibition of attention, flexibility in thinking, and planning. The involvement of the dopaminergic system in cognitive executive functions has been suggested by numerous studies. The aim of the present study was to analyze the effect of cognitive training on cognitive performance of PD-patients ($N=26$). Half of the patients participated in a cognitive training regimen, while the other patients only received standard treatment. The outcome showed improved performance of the group with cognitive treatment in two executive tasks after the training period, while no improvement was seen in the standard-treatment group. The results indicate that specific training is required for improvement of executive functions, while general rehabilitation is not sufficient. Thus, PD-patients might benefit from a short-term cognitive executive function training program that is tailored to the individual patient's needs.

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1. Introduction

The key features of Parkinson's disease (PD) are akinesia, rigidity, tremor and postural instability. However, cognitive and behavioural disturbances are common in PD and often are more disabling than motor manifestations. Examination of cognitive function often reveals mild to moderate deficits, including visuospatial impairment, attentional set-shifting difficulties, working memory impairment and poor executive functions (cp. [1]). The term 'executive functions' refers to a whole range of adaptive abilities such as creative and abstract thought, introspection, forming a plan, based often on recollections of past experience. These abilities play a critical part in complex social behaviour, help to suppress improper actions and to focus on purposeful information [2].

Executive dysfunction underlies all characteristic manifestations of cognitive impairment in PD-patients [3], particularly with higher age and longer duration of the disease [4]. But even in newly diagnosed PD-patients deficits in executive functions including memory were reported [5]. Disturbances of the dopaminergic system are thought to play a role in the development of 'frontal-executive' impairment (see [6]). Altered striatal outflow to the frontal cortex in Parkinson's disease suggests that striatal structures mediate executive functioning [7].

PD-related changes are described in prefrontal regions [8] participating in "cognitive" basal ganglia-thalamocortical circuits [9]. Particularly, orbitofrontal and dorsolateral circuits serve different aspects of executive functioning. The orbitomedial circuit is involved in inhibitory control [4], for instance in the context of task processing within an interfering environment [10], or in the inhibition of ineffective behavioural strategies [11,12]. Dorsolateral activation can frequently be found in working memory tasks, for instance in planning or sequencing tasks [4]. However, the relationship between impaired executive function and altered brain activation is far from being

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established. With executive tasks, hypometabolism (PET) was also found in ventromedial frontal, hippocampal, and striatal areas and hypermetabolism in the mediodorsal thalamus [13]. To summarize, selective cognitive impairment in PD is associated with decrements in working memory that require executive processing, indicating frontal lobe dysfunction.

In a meta-study, substantial evidence was found to support cognitive rehabilitation in traumatic brain injury including strategy training for mild memory impairment [14]. However, to our knowledge there is no model in the literature on impairment of executive function in non-demented PD-patients that allocates specific neuropsychological rehabilitation strategies to executive dysfunction. Therefore cognitive rehabilitation still is considered experimental and investigational for the treatment of cognitive impairment in PD. The aim of the present study was to analyze the effect of cognitive training on cognitive performance of PD-patients. Cognitive function was assessed in 26 idiopathic PD-patients at the beginning and the end of a hospital stay for rehabilitation. Half of the patients underwent cognitive executive function training, while the other patients only received standard treatment, including occupational therapy, physiotherapy, and physical treatment. The training program consisted of a set of working memory tasks requiring executive functions. Based on the results of the preceding diagnostic session, task difficulty was adapted to the individual performance level of the patient.

2. Materials and method

2.1. Subjects

Patients with idiopathic Parkinson's disease were recruited from the 'Parkinson Klinik Bad Nauheim', a hospital specialized in rehabilitation in PD. Twenty-six PD patients (Hoehn and Yahr stages 2–3) were included in the study. All patients were under dopaminergic medication. None of the patients received anticholinergic medication. Twelve patients (age $M=70.8$; $S.D.=7.9$) were randomly allocated to the executive function treatment group; 14 patients formed the standard treatment group (age $M=68.5$; $S.D.=9.0$). Executive function treatment and standard treatment group did not differ in age, severity of disease or cognitive impairment (Mini Mental State $MMS=27.15$; $S.D.=1.49$). Written informed consent was obtained from each patient.

2.2. Neuropsychological testing and training

According to the aim of the study, all patients performed a neuropsychological test battery at the beginning of the 3–4-week hospital stay. The test battery included tests of executive functions (Battery of behavioural assessment of

the Dysexecutive Syndrome BADS, Cognitive Estimation Test TKS, Trail-Making ZVT), working memory (Face–Name-Learning Test GNL), attention ('Alters-Konzentrations-Test' AKT), and well-being ('self rated mood' scale Bf-S). Intelligence and depression were surveyed as control variables using the German test for the assessment of verbal intelligence (MWT) and the Hamilton Rating Scale for Depression (HAMD).

Executive functioning was assessed using two subtests of the 'Battery of behavioural assessment of the Dysexecutive Syndrome' (BADS [15], German version by K. Ufer 2000). The BADS focuses on difficulties in everyday living in the context of the dysexecutive syndrome. The test reveals deficits in patients who normally do not show reduced executive functioning in structured living situations. The subtests selected for this study were the rule-shift cards task and the six-element task. The rule-shift cards task consists of two subtasks, a recognition task ('is red?') and a 1-back task (decision required based on previously presented item), requiring executive functioning ('previous item was red?'). Blocks of these subtasks are presented alternately. The six-element task requires dealing with each element twice within a set time. The same element must not be performed back-to-back.

In the Cognitive Estimation Test (CET) patients are asked to assess quantities that are not readily available to them in their factual knowledge. Patients must make use of strategies to solve the problem (cp. [16]), e.g. to estimate the height of an indoor plant. Appollonio et al. [17] found an impaired cognitive estimation performance in non-demented PD-patients; but they did not find a correlation with executive impairment.

In the framework of executive functions, cognitive flexibility is assessed by the Trail-Making-Test. We used the 'Zahlenverbindungstest' (ZVT) [18], that is a German version of the TMT. This test has two versions. ZVT-A requires the subject to connect a sequence of numbers dispersed across a page as quickly as he/she can without lifting the pen from the paper, and is a simple measure of behavioural regulation and motor speed. In ZVT-B, the subject alternates between sequences of numbers and letters, which requires alternation of mental set. For each version, the time to complete the test is recorded. The difference score of the two versions has been used as an index of behavioural regulation and 'cognitive speed' independent of motor speed.

The Face–Name-Learning Test (GNL) [19] assessed working memory function. 'Face–name' pair associations are learned in four learning-testing trials. Free recall, and cued recall (presentation of faces or names) can be investigated, as well as delayed recall after 30 min. In brain-damaged patients, aspects of the GNL's validity include complex attention, working memory, and intelligence.

Simple attention and vigilance was measured by the 'Alters-Konzentrations-Test' (AKT) [20]. This test is adapted to the performance of the elderly and applicable

to demented subjects as well. Similar to the d2-test, the subjects' task is to mark a target figure within a sequence of similar figures. Speech-skills are not required for this test.

Well-being was assessed using the 'self rated mood' scale (Bf-S) [21]. To control for intelligence score homogeneity of both patient groups, subjects were screened with the 'Mehrfach-Wortschatz-Intelligenztest' (German test for the assessment of verbal intelligence, MWT) [22]. This test probes the vocabulary in ascending difficulty. Depression was measured by the Hamilton Rating Scale for Depression [23]. BADS, AKT, ZVT, GNL (parallel forms) were applied again after the training period.

The treatment group received ten sessions (30 min each) of cognitive training. For the training program a set of working memory tasks requiring executive functions were chosen from a variety of specific tasks. Executive tasks of the BADS (time estimation, visiting a zoo, searching for keys), which were not used for baseline diagnostics, were included in the training. Simple patterns of the 'Raven's Progressive Matrices' were used to establish problem solving strategies in the patients. Picture arrangement tasks, picture completion tasks, block design, and object assembly (jigsaw type puzzles) were adapted from the 'Wechsler Intelligence test for children'. Speech production was encouraged by requesting patients to tell short stories or to discuss short text-passages. Similar to the GNL, a set of photos was used for training of working memory and for producing short stories based on those pictures. All training methods were designed to improve working memory abilities associated with executive functions. Based on the results of the previous baseline diagnostic session, task difficulty was adapted to the individual performance level of the patients.

3. Results

Neuropsychological testing data were analyzed using repeated measurement analysis of variance. The repeated measurement factor in the ANOVA was 'baseline testing vs. outcome testing'; group factor was 'patients vs. control subjects'.

While there was no difference between groups in the AKT, ZVT and both BADS subtests in the baseline measurement, the executive function treatment group was superior to the standard treatment group in the face-name learning test ($F(1,24)=6.49$; $p<.0177$).

Fig. 1 shows the neuropsychological test results representing executive functions in the cognitive executive function-training group (upper graph) and the standard treatment group (lower graph). Neither for the executive function-training group nor for the standard treatment patient group were significant differences found in the AKT, the ZVT time for completion, and the ZVT errors. However, patients in the executive function treatment group

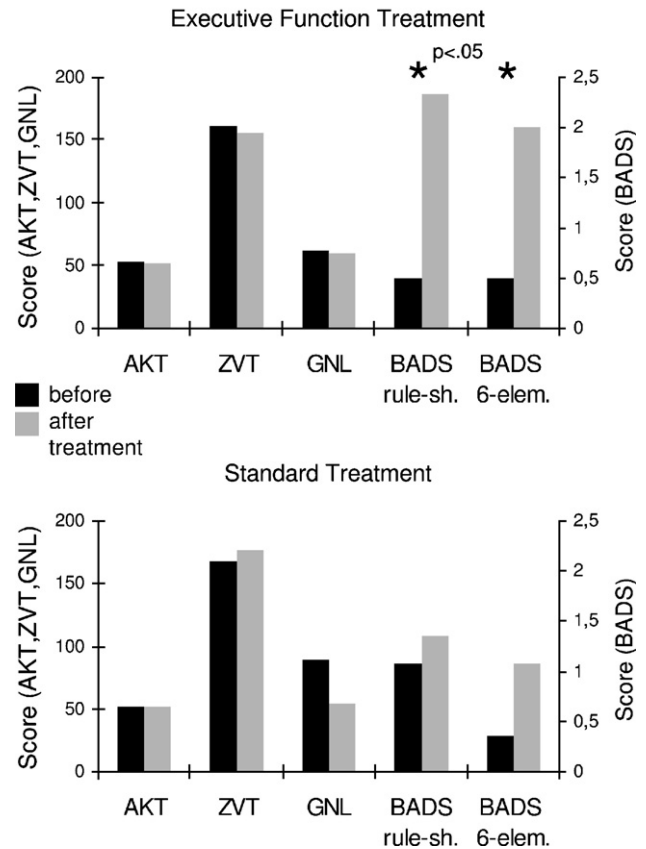


Fig. 1. Results of the neuropsychological tests of executive functions in the executive function training group (upper graph) and the standard treatment group (lower graph). Test scores are displayed for the AKT (attention), ZVT (trail-making), GNL (face-name learning), rule shift task and six-element task of the BADS. Both BADS are scaled separately (right y-axis). Black bars represent the neuropsychological testing before the treatment. The after treatment assessment is indicated by gray bars. Statistically significant differences at $p<.05$ are indicated by '*'.

improved significantly in both tasks of the 'Battery of behavioural assessment of the Dysexecutive Syndrome' (BADS). These patients performed significantly better in the rule shift task than non-specifically trained patients ($F(1,24)=4.98$; $p<.035$). Patients in both groups improved in the six-element task after treatment ($F(1,24)=20.08$; $p<.0002$). However, the performance of the cognitively treated patient group tended to be superior to the patients without specific treatment ($F(1,24)=2.53$; $p<.12$). The recall of face-name pairs after 30 min dropped from the baseline measurement to the second neuropsychological testing. This reduced performance on test repetition was not expected and not reported to occur with parallel form testing in the literature before. Interestingly, while the training group could maintain their level of performance, the control group recalled fewer items 30 min after memorizing them ($F(1,24)=6.49$; $p<.02$). Due to the lower performance level of the executive function treatment group in the baseline measurement compared to the standard treatment group, the difference at the second measurement failed to reach statistical significance (Fig. 1).

Table 1

Test–retest correlations for the executive function treatment group and the standard treatment group

Test–retest correlation	AKT	ZVT	GNL	BADS instruction shift	BADS 6-element task
Executive function treatment	<i>r</i> = .019 <i>p</i> = .954	<i>r</i> = .752 <i>p</i> = .005	<i>r</i> = .593 <i>p</i> = .042	<i>r</i> = .112 <i>p</i> = .728	<i>r</i> = .270 <i>p</i> = .397
Standard treatment	<i>r</i> = .506 <i>p</i> = .065	<i>r</i> = .595 <i>p</i> = .025	<i>r</i> = .307 <i>p</i> = .285	<i>r</i> = .352 <i>p</i> = .217	<i>r</i> = .525 <i>p</i> = .054

Bold print indicates significant correlation coefficients at $p < .05$.

Test–retest correlations were of low to medium height (Table 1). Significant correlations were found for the ZVT in both groups, the GNL in the executive function training group, and a medium correlation was found for the six-element task in the standard treatment group.

No differences between the groups were found concerning intelligence, depression, or subjective condition.

4. Discussion

The main finding of the current study was an improved performance in patients who received cognitive treatment in tasks associated with core executive abilities: rule shift, and organizing performance of a task, which required a switch between several sub-tasks. Patients who received standard treatment did not show a statistically significant improvement in these tasks. While subjects who received standard treatment initially had higher scores in the face–name learning test prior to the treatment, the performance in this test dropped at the second measurement. However, executive function treatment group patients could maintain their performance in the after-treatment measurement. When organizing a task by switching between several sub-tasks, the standard treatment group showed a slightly enhanced performance in the second measurement, but this tendency failed to reach statistical significance. It should be noted that BADS scale range is only zero to four (in whole numbers) limiting the variability of the scores and accordingly attenuating correlation measurement. However, the usage of BADS raw values bears the disadvantage of making the results less comparable to those of other studies.

Test–retest correlation coefficients ranged from low to medium values. Medium correlation coefficients for trail making in both groups and for face–name learning in the executive function treatment group indicated stability of test performance. In the standard treatment group, test–retest correlations were nearly significant for attention (AKT) and executive function (six-element test). The lowest correlations were found for attention and both BADS subtests, revealing a higher rate of change from before to after the treatment in executive function trained subjects.

Limitations of the study were the relatively small sample size. Furthermore, we had no opportunity to test for transfer effects in everyday life of the participating patients. In principle, the individual but highly structured executive skill

training procedure can be applied to the patient with the help of a trained layperson.

To our knowledge there are no systematic studies on cognitive rehabilitation in cognitively impaired PD-patients. In general, there are only few studies on cognitive remediation of executive functioning, mainly in the area of acquired brain injury. These studies provided evidence for the benefit of cognitive rehabilitation techniques compared to no treatment or standard treatment [14]. The number of studies is small, and both the methods and results of those studies seem to be inconsistent; however, it appears that patients can benefit from additional cognitive rehabilitation. The results of the current study are in line with the effects of cognitive rehabilitation in other diseases or acquired brain injury. With regard to all limitations of this study, the results suggest that a short but specific training promotes improvement in some aspects of the patient's executive functioning. The specificity of the cognitive treatment is demonstrated by the fact that other cognitive functional domains such as vigilance and attention were not improved by the cognitive training or by the non-specific standard treatment. In addition, depression, intelligence and other variables did not interact with the impact of the training regimen.

In conclusion, PD-patients appear to benefit from a specific short-term training of cognitive executive function that is tailored to the patient's needs. The impairment of executive functions in PD is in accord with the pathological findings. The destruction of the nigrostriatal dopaminergic system is often greater than 75% and involves degeneration in the ventral tegmental area, which innervates the prefrontal cortex. Since Hoehn and Yahr stages did not differ between treated and non-treated patients, differences in the severity of the disease did not account for differences in cognitive performance. Cognitive training does not change the neurotransmitter status in the brain and is unlikely to reconstruct damaged pathways. Other resources might be used for improvement in subtasks of executive function tests. Although the mechanisms of cognitive training are not clear yet, the current results show that specific training is required for improvement and that general rehabilitation is not sufficient to improve cognitive functions. Systematic studies on how to individually compose and apply cognitive training strategies need to be developed. Further assessments are necessary to evaluate whether the observed test improvements can be translated into improved functioning in everyday living.

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